



STUDY	DISEASE	PARTICIPANT	REPORT DATE	REPORT STATUS
haib20SL6185	Uncertain diagnosis	6185-SL-0046		Final

### CLINICALLY RELEVANT RESULTS

## Tier I - Strong Clinical Significance

No variants were reported for this classification tier.

## Tier II - Potential Clinical Significance

VARIANT	CLINICAL IMPACT
<p><b>TPM3, NTRK1</b></p> <p>TPM3-NTRK1 fusion transcript</p> <p>C</p>	<p><b>May benefit from</b></p> <ul style="list-style-type: none"> <li>— Bevacizumab-bvzr, Bevacizumab-awwb, Bevacizumab, or Atezolizumab <i>in Nonsquamous non-small cell neoplasm of lung, Adenocarcinoma of lung, or Large cell carcinoma of lung</i></li> <li>— Pembrolizumab or Ipilimumab + Nivolumab <i>in Squamous cell carcinoma of lung, Adenocarcinoma of lung, Non-small cell lung cancer, Large cell carcinoma of lung, or Non-small cell carcinoma</i></li> <li>— Larotrectinib <i>in Malignant tumor of colon, Malignant tumor of lung, Invasive micropapillary carcinoma of breast, Carcinoma of salivary gland type, Endometrial carcinoma, Desmoplastic malignant melanoma, Anaplastic thyroid carcinoma, Siewert type II adenocarcinoma of esophagogastric junction, Adenocarcinoma of cervix, Nodular malignant melanoma of skin, Adenocarcinoma of pancreas, Sarcoma of soft tissue, Adenocarcinoma of lung, Primary adenocarcinoma of colon, Malignant tumor of fallopian tube, Squamous cell carcinoma of vulva, Adenocarcinoma of rectum, Infiltrating lobular carcinoma of breast, Malignant tumor of ovary, Malignant tumor of rectum, Malignant tumor of thyroid gland, Infantile fibrosarcoma, Mixed ductal and lobular carcinoma of breast, High grade endometrial stromal sarcoma, Adenocarcinoma of small intestine, Non-small cell carcinoma, Hurthle cell carcinoma of thyroid, Malignant tumor of esophagus, Non-small cell lung cancer, Malignant tumor of appendix, Adenocarcinoma of esophagus, Acral lentiginous malignant melanoma of skin, Undifferentiated sarcoma, Infiltrating carcinoma with ductal and lobular features, Malignant tumor of salivary gland, Malignant melanoma of skin, Primary</i></li> </ul>

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VARIANT	CLINICAL IMPACT
	<p><i>malignant neoplasm of cystic duct, Squamous cell carcinoma of lung, Squamous cell carcinoma of esophagus, Glioblastoma, Hepatocellular carcinoma, Malignant tumor of pancreas, Gastrointestinal stromal tumor, Malignant epithelial tumor of ovary, Lentigo maligna, Leiomyosarcoma of uterus, Malignant tumor of breast, Primary malignant neoplasm of distal bile duct, Infiltrating duct carcinoma of breast, Follicular thyroid carcinoma, Malignant neoplasm of intrahepatic gall duct, Superficial spreading malignant melanoma of skin, Malignant melanoma, Malignant tumor of cervix, Inflammatory carcinoma of breast, Large cell carcinoma of lung, Cholangiocarcinoma, Primary malignant neoplasm of the peritoneum, Astrocytoma of brain, Superficial spreading melanoma, Carcinoma of esophagus, Klatskin's tumor, Siewert type III adenocarcinoma of esophagogastric junction, Malignant tumor of gallbladder, Primary malignant neoplasm of perihilar bile duct, Cholangiocarcinoma of biliary tract, Siewert type I adenocarcinoma of esophagogastric junction, Primary malignant clear cell tumor of ovary, Carcinosarcoma of ovary, Malignant tumor of stomach, Glioma, Squamous cell carcinoma of cervix, Endometrioid carcinoma, Nodular melanoma, Adenosquamous carcinoma of cervix, Endometrioid carcinoma ovary, Mucinous carcinoma of breast, Adenocarcinoma of stomach, or Papillary thyroid carcinoma</i></p> <p>— <i>Entrectinib in Malignant tumor of colon, Invasive micropapillary carcinoma of breast, Carcinoma of salivary gland type, Desmoplastic malignant melanoma, Endometrial carcinoma, Anaplastic thyroid carcinoma, Siewert type II adenocarcinoma of esophagogastric junction, Adenocarcinoma of cervix, Nodular malignant melanoma of skin, Adenocarcinoma of pancreas, Sarcoma of soft tissue, Adenocarcinoma of lung, Malignant tumor of vulva, Primary adenocarcinoma of colon, Malignant tumor of fallopian tube, Squamous cell carcinoma of vulva, Adenocarcinoma of rectum, Infiltrating lobular carcinoma of breast, Malignant tumor of ovary, Malignant tumor of rectum, Malignant neoplasm of endometrium of corpus uteri, Malignant tumor of thyroid gland, High grade endometrial stromal sarcoma, Mixed ductal and lobular carcinoma of breast, Non-small cell carcinoma, Hurthle cell carcinoma of thyroid, Neuroendocrine carcinoma, Malignant tumor of esophagus, Non-small cell lung cancer, Acral lentiginous malignant melanoma of skin, Adenocarcinoma of esophagus, Undifferentiated sarcoma, Malignant tumor of vagina, Infiltrating carcinoma with ductal and lobular features, Malignant tumor of salivary gland, Malignant neoplasm of uterus, Malignant melanoma of skin, Primary malignant neoplasm of cystic duct, Squamous cell carcinoma of lung, Squamous cell carcinoma of esophagus, Hepatocellular carcinoma, Malignant tumor of pancreas, Gastrointestinal stromal tumor, Malignant epithelial tumor of ovary, Lentigo maligna, Leiomyosarcoma of uterus, Malignant tumor of breast, Primary malignant neoplasm of distal bile duct, Follicular thyroid carcinoma, Malignant neoplasm of intrahepatic gall duct, Infiltrating duct carcinoma of breast, Superficial spreading malignant melanoma of skin,</i></p>

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VARIANT

CLINICAL IMPACT

*Malignant tumor of cervix, Inflammatory carcinoma of breast, Large cell carcinoma of lung, Cholangiocarcinoma, Primary malignant neoplasm of the peritoneum, Superficial spreading melanoma, Carcinoma of esophagus, Klatskin's tumor, Sarcoma, Siewert type III adenocarcinoma of esophagogastric junction, Malignant tumor of gallbladder, Primary malignant neoplasm of perihilar bile duct, Siewert type I adenocarcinoma of esophagogastric junction, Primary malignant clear cell tumor of ovary, Carcinosarcoma of ovary, Malignant tumor of stomach, Squamous cell carcinoma of cervix, Endometrioid carcinoma, Nodular melanoma, Adenosquamous carcinoma of cervix, Endometrioid carcinoma ovary, Adenocarcinoma of stomach, Mucinous carcinoma of breast, or Papillary thyroid carcinoma*

INTERPRETATION

(1) The FDA recently approved larotrectinib and entrectinib for treatment of patients with NTRK gene fusion-positive tumors, and the panel also recommends NTRK therapy options such as larotrectinib and entrectinib for patients with recurrent NTRK gene fusion-positive salivary gland tumors and distant metastases. (2) NTRK status should be evaluated in mammary analogue secretory carcinoma of the salivary gland. (3) Useful in certain circumstances as single-agent systemic therapy for NTRK gene fusion-positive recurrent disease with (a) distant metastases in patients with a performance status (PS) of 0-3, (b) unresectable locoregional recurrence or second primary with prior radiation therapy.

**LMNA, NTRK1**

LMNA-NTRK1  
fusion transcript

C

**May benefit from**

- Bevacizumab-bvzr, Bevacizumab-awwb, Bevacizumab, or Atezolizumab *in Nonsquamous non-small cell neoplasm of lung, Adenocarcinoma of lung, or Large cell carcinoma of lung*
- Pembrolizumab or Ipilimumab + Nivolumab *in Squamous cell carcinoma of lung, Adenocarcinoma of lung, Non-small cell lung cancer, Large cell carcinoma of lung, or Non-small cell carcinoma*
- Larotrectinib *in Malignant tumor of colon, Malignant tumor of lung, Invasive micropapillary carcinoma of breast, Carcinoma of salivary gland type, Endometrial carcinoma, Desmoplastic malignant melanoma, Anaplastic thyroid carcinoma, Siewert type II adenocarcinoma of esophagogastric junction, Adenocarcinoma of cervix, Nodular malignant melanoma of skin, Adenocarcinoma of pancreas, Sarcoma of soft tissue, Adenocarcinoma of lung, Primary adenocarcinoma of colon, Malignant tumor of fallopian tube, Squamous cell carcinoma of vulva, Adenocarcinoma of rectum, Infiltrating lobular carcinoma of breast, Malignant tumor of ovary, Malignant tumor of*

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	<p><i>rectum, Malignant tumor of thyroid gland, Infantile fibrosarcoma, Mixed ductal and lobular carcinoma of breast, High grade endometrial stromal sarcoma, Adenocarcinoma of small intestine, Non-small cell carcinoma, Hurthle cell carcinoma of thyroid, Malignant tumor of esophagus, Non-small cell lung cancer, Malignant tumor of appendix, Adenocarcinoma of esophagus, Acral lentiginous malignant melanoma of skin, Undifferentiated sarcoma, Infiltrating carcinoma with ductal and lobular features, Malignant tumor of salivary gland, Malignant melanoma of skin, Primary malignant neoplasm of cystic duct, Squamous cell carcinoma of lung, Squamous cell carcinoma of esophagus, Glioblastoma, Hepatocellular carcinoma, Malignant tumor of pancreas, Gastrointestinal stromal tumor, Malignant epithelial tumor of ovary, Lentigo maligna, Leiomyosarcoma of uterus, Malignant tumor of breast, Primary malignant neoplasm of distal bile duct, Infiltrating duct carcinoma of breast, Follicular thyroid carcinoma, Malignant neoplasm of intrahepatic gall duct, Superficial spreading malignant melanoma of skin, Malignant melanoma, Malignant tumor of cervix, Inflammatory carcinoma of breast, Large cell carcinoma of lung, Cholangiocarcinoma, Primary malignant neoplasm of the peritoneum, Astrocytoma of brain, Superficial spreading melanoma, Carcinoma of esophagus, Klatskin's tumor, Siewert type III adenocarcinoma of esophagogastric junction, Malignant tumor of gallbladder, Primary malignant neoplasm of perihilar bile duct, Cholangiocarcinoma of biliary tract, Siewert type I adenocarcinoma of esophagogastric junction, Primary malignant clear cell tumor of ovary, Carcinosarcoma of ovary, Malignant tumor of stomach, Glioma, Squamous cell carcinoma of cervix, Endometrioid carcinoma, Nodular melanoma, Adenosquamous carcinoma of cervix, Endometrioid carcinoma ovary, Mucinous carcinoma of breast, Adenocarcinoma of stomach, or Papillary thyroid carcinoma</i></p> <p>— <i>Entrectinib in Malignant tumor of colon, Invasive micropapillary carcinoma of breast, Carcinoma of salivary gland type, Desmoplastic malignant melanoma, Endometrial carcinoma, Anaplastic thyroid carcinoma, Siewert type II adenocarcinoma of esophagogastric junction, Adenocarcinoma of cervix, Nodular malignant melanoma of skin, Adenocarcinoma of pancreas, Sarcoma of soft tissue, Adenocarcinoma of lung, Malignant tumor of vulva, Primary adenocarcinoma of colon, Malignant tumor of fallopian tube, Squamous cell carcinoma of vulva, Adenocarcinoma of rectum, Infiltrating lobular carcinoma of breast, Malignant tumor of ovary, Malignant tumor of rectum, Malignant neoplasm of endometrium of corpus uteri, Malignant tumor of thyroid gland, High grade endometrial stromal sarcoma, Mixed ductal and lobular carcinoma of breast, Non-small cell carcinoma, Hurthle cell carcinoma of thyroid, Neuroendocrine carcinoma, Malignant tumor of esophagus, Non-small cell lung cancer, Acral lentiginous malignant melanoma of skin, Adenocarcinoma of esophagus, Undifferentiated sarcoma, Malignant tumor of vagina, Infiltrating carcinoma with ductal and lobular features, Malignant tumor of salivary gland, Malignant neoplasm of</i></p>

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VARIANT

CLINICAL IMPACT

*uterus, Malignant melanoma of skin, Primary malignant neoplasm of cystic duct, Squamous cell carcinoma of lung, Squamous cell carcinoma of esophagus, Hepatocellular carcinoma, Malignant tumor of pancreas, Gastrointestinal stromal tumor, Malignant epithelial tumor of ovary, Lentigo maligna, Leiomyosarcoma of uterus, Malignant tumor of breast, Primary malignant neoplasm of distal bile duct, Follicular thyroid carcinoma, Malignant neoplasm of intrahepatic gall duct, Infiltrating duct carcinoma of breast, Superficial spreading malignant melanoma of skin, Malignant tumor of cervix, Inflammatory carcinoma of breast, Large cell carcinoma of lung, Cholangiocarcinoma, Primary malignant neoplasm of the peritoneum, Superficial spreading melanoma, Carcinoma of esophagus, Klatskin's tumor, Sarcoma, Siewert type III adenocarcinoma of esophagogastric junction, Malignant tumor of gallbladder, Primary malignant neoplasm of perihilar bile duct, Siewert type I adenocarcinoma of esophagogastric junction, Primary malignant clear cell tumor of ovary, Carcinosarcoma of ovary, Malignant tumor of stomach, Squamous cell carcinoma of cervix, Endometrioid carcinoma, Nodular melanoma, Adenosquamous carcinoma of cervix, Endometrioid carcinoma ovary, Adenocarcinoma of stomach, Mucinous carcinoma of breast, or Papillary thyroid carcinoma*

INTERPRETATION

(1) The FDA recently approved larotrectinib and entrectinib for treatment of patients with NTRK gene fusion-positive tumors, and the panel also recommends NTRK therapy options such as larotrectinib and entrectinib for patients with recurrent NTRK gene fusion-positive salivary gland tumors and distant metastases. (2) NTRK status should be evaluated in mammary analogue secretory carcinoma of the salivary gland. (3) Useful in certain circumstances as single-agent systemic therapy for NTRK gene fusion-positive recurrent disease with (a) distant metastases in patients with a performance status (PS) of 0-3, (b) unresectable locoregional recurrence or second primary with prior radiation therapy.

**TRIM24, NTRK2**

TRIM24-NTRK2  
fusion transcript

C

**May benefit from**

- Bevacizumab-bvzr, Bevacizumab-awwb, Bevacizumab, or Atezolizumab *in Nonsquamous non-small cell neoplasm of lung, Adenocarcinoma of lung, or Large cell carcinoma of lung*
- Pembrolizumab or Ipilimumab + Nivolumab *in Squamous cell carcinoma of lung, Adenocarcinoma of lung, Non-small cell lung cancer, Large cell carcinoma of lung, or Non-small cell carcinoma*

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	<p>— Larotrectinib in <i>Malignant tumor of colon, Malignant tumor of lung, Invasive micropapillary carcinoma of breast, Carcinoma of salivary gland type, Endometrial carcinoma, Desmoplastic malignant melanoma, Anaplastic thyroid carcinoma, Siewert type II adenocarcinoma of esophagogastric junction, Adenocarcinoma of cervix, Nodular malignant melanoma of skin, Adenocarcinoma of pancreas, Sarcoma of soft tissue, Adenocarcinoma of lung, Primary adenocarcinoma of colon, Malignant tumor of fallopian tube, Squamous cell carcinoma of vulva, Adenocarcinoma of rectum, Infiltrating lobular carcinoma of breast, Malignant tumor of ovary, Malignant tumor of rectum, Malignant tumor of thyroid gland, Infantile fibrosarcoma, Mixed ductal and lobular carcinoma of breast, High grade endometrial stromal sarcoma, Adenocarcinoma of small intestine, Non-small cell carcinoma, Hurthle cell carcinoma of thyroid, Malignant tumor of esophagus, Non-small cell lung cancer, Malignant tumor of appendix, Acral lentiginous malignant melanoma of skin, Adenocarcinoma of esophagus, Undifferentiated sarcoma, Infiltrating carcinoma with ductal and lobular features, Malignant tumor of salivary gland, Malignant melanoma of skin, Primary malignant neoplasm of cystic duct, Squamous cell carcinoma of lung, Squamous cell carcinoma of esophagus, Glioblastoma, Hepatocellular carcinoma, Malignant tumor of pancreas, Gastrointestinal stromal tumor, Malignant epithelial tumor of ovary, Lentigo maligna, Leiomyosarcoma of uterus, Malignant tumor of breast, Primary malignant neoplasm of distal bile duct, Infiltrating duct carcinoma of breast, Follicular thyroid carcinoma, Malignant neoplasm of intrahepatic gall duct, Superficial spreading malignant melanoma of skin, Malignant melanoma, Malignant tumor of cervix, Inflammatory carcinoma of breast, Large cell carcinoma of lung, Cholangiocarcinoma, Primary malignant neoplasm of the peritoneum, Astrocytoma of brain, Superficial spreading melanoma, Carcinoma of esophagus, Klatskin's tumor, Siewert type III adenocarcinoma of esophagogastric junction, Malignant tumor of gallbladder, Primary malignant neoplasm of perihilar bile duct, Cholangiocarcinoma of biliary tract, Siewert type I adenocarcinoma of esophagogastric junction, Primary malignant clear cell tumor of ovary, Carcinosarcoma of ovary, Malignant tumor of stomach, Glioma, Squamous cell carcinoma of cervix, Endometrioid carcinoma, Nodular melanoma, Adenosquamous carcinoma of cervix, Endometrioid carcinoma ovary, Mucinous carcinoma of breast, Adenocarcinoma of stomach, or Papillary thyroid carcinoma</i></p> <p>— Entrectinib in <i>Malignant tumor of colon, Invasive micropapillary carcinoma of breast, Carcinoma of salivary gland type, Desmoplastic malignant melanoma, Endometrial carcinoma, Anaplastic thyroid carcinoma, Siewert type II adenocarcinoma of esophagogastric junction, Adenocarcinoma of cervix, Nodular malignant melanoma of skin, Adenocarcinoma of pancreas, Sarcoma of soft tissue, Adenocarcinoma of lung, Malignant tumor of vulva, Primary adenocarcinoma of colon, Malignant tumor of fallopian tube, Squamous cell carcinoma of vulva, Adenocarcinoma of rectum,</i></p>

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VARIANT

CLINICAL IMPACT

*Infiltrating lobular carcinoma of breast, Malignant tumor of ovary, Malignant tumor of rectum, Malignant neoplasm of endometrium of corpus uteri, Malignant tumor of thyroid gland, High grade endometrial stromal sarcoma, Mixed ductal and lobular carcinoma of breast, Non-small cell carcinoma, Hurthle cell carcinoma of thyroid, Neuroendocrine carcinoma, Malignant tumor of esophagus, Non-small cell lung cancer, Acral lentiginous malignant melanoma of skin, Adenocarcinoma of esophagus, Undifferentiated sarcoma, Malignant tumor of vagina, Infiltrating carcinoma with ductal and lobular features, Malignant tumor of salivary gland, Malignant neoplasm of uterus, Malignant melanoma of skin, Primary malignant neoplasm of cystic duct, Squamous cell carcinoma of lung, Squamous cell carcinoma of esophagus, Hepatocellular carcinoma, Malignant tumor of pancreas, Gastrointestinal stromal tumor, Malignant epithelial tumor of ovary, Lentigo maligna, Leiomyosarcoma of uterus, Malignant tumor of breast, Primary malignant neoplasm of distal bile duct, Follicular thyroid carcinoma, Malignant neoplasm of intrahepatic gall duct, Infiltrating duct carcinoma of breast, Superficial spreading malignant melanoma of skin, Malignant tumor of cervix, Inflammatory carcinoma of breast, Large cell carcinoma of lung, Cholangiocarcinoma, Primary malignant neoplasm of the peritoneum, Superficial spreading melanoma, Carcinoma of esophagus, Klatskin's tumor, Sarcoma, Siewert type III adenocarcinoma of esophagogastric junction, Malignant tumor of gallbladder, Primary malignant neoplasm of perihilar bile duct, Siewert type I adenocarcinoma of esophagogastric junction, Primary malignant clear cell tumor of ovary, Carcinosarcoma of ovary, Malignant tumor of stomach, Squamous cell carcinoma of cervix, Endometrioid carcinoma, Nodular melanoma, Adenosquamous carcinoma of cervix, Endometrioid carcinoma ovary, Adenocarcinoma of stomach, Mucinous carcinoma of breast, or Papillary thyroid carcinoma*

INTERPRETATION

(1) The FDA recently approved larotrectinib and entrectinib for treatment of patients with NTRK gene fusion-positive tumors, and the panel also recommends NTRK therapy options such as larotrectinib and entrectinib for patients with recurrent NTRK gene fusion-positive salivary gland tumors and distant metastases. (2) NTRK status should be evaluated in mammary analogue secretory carcinoma of the salivary gland. (3) Useful in certain circumstances as single-agent systemic therapy for NTRK gene fusion-positive recurrent disease with (a) distant metastases in patients with a performance status (PS) of 0-3, (b) unresectable locoregional recurrence or second primary with prior radiation therapy.

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<p><b>SQSTM1, NTRK1</b></p> <p>SQSTM1-NTRK1 fusion transcript</p> <p>C</p>	<p><b>May benefit from</b></p> <ul style="list-style-type: none"> <li>— Bevacizumab-bvzr, Bevacizumab-awwb, Bevacizumab, or Atezolizumab in <i>Nonsquamous nonsmall cell neoplasm of lung, Adenocarcinoma of lung, or Large cell carcinoma of lung</i></li> <li>— Pembrolizumab or Ipilimumab + Nivolumab in <i>Squamous cell carcinoma of lung, Adenocarcinoma of lung, Non-small cell lung cancer, Large cell carcinoma of lung, or Non-small cell carcinoma</i></li> <li>— Larotrectinib in <i>Malignant tumor of colon, Malignant tumor of lung, Invasive micropapillary carcinoma of breast, Carcinoma of salivary gland type, Endometrial carcinoma, Desmoplastic malignant melanoma, Anaplastic thyroid carcinoma, Siewert type II adenocarcinoma of esophagogastric junction, Adenocarcinoma of cervix, Nodular malignant melanoma of skin, Adenocarcinoma of pancreas, Sarcoma of soft tissue, Adenocarcinoma of lung, Primary adenocarcinoma of colon, Malignant tumor of fallopian tube, Squamous cell carcinoma of vulva, Adenocarcinoma of rectum, Infiltrating lobular carcinoma of breast, Malignant tumor of ovary, Malignant tumor of rectum, Malignant tumor of thyroid gland, Infantile fibrosarcoma, Mixed ductal and lobular carcinoma of breast, High grade endometrial stromal sarcoma, Adenocarcinoma of small intestine, Non-small cell carcinoma, Hurthle cell carcinoma of thyroid, Malignant tumor of esophagus, Non-small cell lung cancer, Malignant tumor of appendix, Adenocarcinoma of esophagus, Acral lentiginous malignant melanoma of skin, Undifferentiated sarcoma, Infiltrating carcinoma with ductal and lobular features, Malignant tumor of salivary gland, Malignant melanoma of skin, Primary malignant neoplasm of cystic duct, Squamous cell carcinoma of lung, Squamous cell carcinoma of esophagus, Glioblastoma, Hepatocellular carcinoma, Malignant tumor of pancreas, Gastrointestinal stromal tumor, Malignant epithelial tumor of ovary, Lentigo maligna, Leiomyosarcoma of uterus, Malignant tumor of breast, Primary malignant neoplasm of distal bile duct, Infiltrating duct carcinoma of breast, Follicular thyroid carcinoma, Malignant neoplasm of intrahepatic gall duct, Superficial spreading malignant melanoma of skin, Malignant melanoma, Malignant tumor of cervix, Inflammatory carcinoma of breast, Large cell carcinoma of lung, Cholangiocarcinoma, Primary malignant neoplasm of the peritoneum, Astrocytoma of brain, Superficial spreading melanoma, Carcinoma of esophagus, Klatskin's tumor, Siewert type III adenocarcinoma of esophagogastric junction, Malignant tumor of gallbladder, Primary malignant neoplasm of perihilar bile duct, Cholangiocarcinoma of biliary tract, Siewert type I adenocarcinoma of esophagogastric junction, Primary malignant clear cell tumor of ovary, Carcinosarcoma of ovary, Malignant tumor of stomach, Glioma, Squamous cell carcinoma of cervix, Endometrioid carcinoma, Nodular melanoma, Adenosquamous carcinoma of cervix, Endometrioid carcinoma ovary,</i></li> </ul>



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	<p><i>Mucinous carcinoma of breast, Adenocarcinoma of stomach, or Papillary thyroid carcinoma</i></p> <p>— Entrectinib in <i>Malignant tumor of colon, Invasive micropapillary carcinoma of breast, Carcinoma of salivary gland type, Desmoplastic malignant melanoma, Endometrial carcinoma, Anaplastic thyroid carcinoma, Siewert type II adenocarcinoma of esophagogastric junction, Adenocarcinoma of cervix, Nodular malignant melanoma of skin, Adenocarcinoma of pancreas, Sarcoma of soft tissue, Adenocarcinoma of lung, Malignant tumor of vulva, Primary adenocarcinoma of colon, Malignant tumor of fallopian tube, Squamous cell carcinoma of vulva, Adenocarcinoma of rectum, Infiltrating lobular carcinoma of breast, Malignant tumor of ovary, Malignant tumor of rectum, Malignant neoplasm of endometrium of corpus uteri, Malignant tumor of thyroid gland, High grade endometrial stromal sarcoma, Mixed ductal and lobular carcinoma of breast, Non-small cell carcinoma, Hurthle cell carcinoma of thyroid, Neuroendocrine carcinoma, Malignant tumor of esophagus, Non-small cell lung cancer, Acral lentiginous malignant melanoma of skin, Adenocarcinoma of esophagus, Undifferentiated sarcoma, Malignant tumor of vagina, Infiltrating carcinoma with ductal and lobular features, Malignant tumor of salivary gland, Malignant neoplasm of uterus, Malignant melanoma of skin, Primary malignant neoplasm of cystic duct, Squamous cell carcinoma of lung, Squamous cell carcinoma of esophagus, Hepatocellular carcinoma, Malignant tumor of pancreas, Gastrointestinal stromal tumor, Malignant epithelial tumor of ovary, Lentigo maligna, Leiomyosarcoma of uterus, Malignant tumor of breast, Primary malignant neoplasm of distal bile duct, Follicular thyroid carcinoma, Malignant neoplasm of intrahepatic gall duct, Infiltrating duct carcinoma of breast, Superficial spreading malignant melanoma of skin, Malignant tumor of cervix, Inflammatory carcinoma of breast, Large cell carcinoma of lung, Cholangiocarcinoma, Primary malignant neoplasm of the peritoneum, Superficial spreading melanoma, Carcinoma of esophagus, Klatskin's tumor, Sarcoma, Siewert type III adenocarcinoma of esophagogastric junction, Malignant tumor of gallbladder, Primary malignant neoplasm of perihilar bile duct, Siewert type I adenocarcinoma of esophagogastric junction, Primary malignant clear cell tumor of ovary, Carcinosarcoma of ovary, Malignant tumor of stomach, Squamous cell carcinoma of cervix, Endometrioid carcinoma, Nodular melanoma, Adenosquamous carcinoma of cervix, Endometrioid carcinoma ovary, Adenocarcinoma of stomach, Mucinous carcinoma of breast, or Papillary thyroid carcinoma</i></p>

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INTERPRETATION

(1) The FDA recently approved larotrectinib and entrectinib for treatment of patients with NTRK gene fusion-positive tumors, and the panel also recommends NTRK therapy options such as larotrectinib and entrectinib for patients with recurrent NTRK gene fusion-positive salivary gland tumors and distant metastases. (2) NTRK status should be evaluated in mammary analogue secretory carcinoma of the salivary gland. (3) Useful in certain circumstances as single-agent systemic therapy for NTRK gene fusion-positive recurrent disease with (a) distant metastases in patients with a performance status (PS) of 0-3, (b) unresectable locoregional recurrence or second primary with prior radiation therapy.

**IRF2BP2, NTRK1**

IRF2BP2-NTRK1  
fusion transcript

C

**May benefit from**

- Bevacizumab-bvzr, Bevacizumab-awwb, Bevacizumab, or Atezolizumab *in Nonsquamous non-small cell neoplasm of lung, Adenocarcinoma of lung, or Large cell carcinoma of lung*
- Pembrolizumab or Ipilimumab + Nivolumab *in Squamous cell carcinoma of lung, Adenocarcinoma of lung, Non-small cell lung cancer, Large cell carcinoma of lung, or Non-small cell carcinoma*
- Larotrectinib *in Malignant tumor of colon, Malignant tumor of lung, Invasive micropapillary carcinoma of breast, Carcinoma of salivary gland type, Endometrial carcinoma, Desmoplastic malignant melanoma, Anaplastic thyroid carcinoma, Siewert type II adenocarcinoma of esophagogastric junction, Adenocarcinoma of cervix, Nodular malignant melanoma of skin, Adenocarcinoma of pancreas, Sarcoma of soft tissue, Adenocarcinoma of lung, Primary adenocarcinoma of colon, Malignant tumor of fallopian tube, Squamous cell carcinoma of vulva, Adenocarcinoma of rectum, Infiltrating lobular carcinoma of breast, Malignant tumor of ovary, Malignant tumor of rectum, Malignant tumor of thyroid gland, Infantile fibrosarcoma, Mixed ductal and lobular carcinoma of breast, High grade endometrial stromal sarcoma, Adenocarcinoma of small intestine, Non-small cell carcinoma, Hurthle cell carcinoma of thyroid, Malignant tumor of esophagus, Non-small cell lung cancer, Malignant tumor of appendix, Adenocarcinoma of esophagus, Acral lentiginous malignant melanoma of skin, Undifferentiated sarcoma, Infiltrating carcinoma with ductal and lobular features, Malignant tumor of salivary gland, Malignant melanoma of skin, Primary malignant neoplasm of cystic duct, Squamous cell carcinoma of lung, Squamous cell carcinoma of esophagus, Glioblastoma, Hepatocellular carcinoma, Malignant tumor of pancreas, Gastrointestinal stromal tumor, Malignant epithelial tumor of ovary, Lentigo*

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	<p><i>maligna, Leiomyosarcoma of uterus, Malignant tumor of breast, Primary malignant neoplasm of distal bile duct, Infiltrating duct carcinoma of breast, Follicular thyroid carcinoma, Malignant neoplasm of intrahepatic gall duct, Superficial spreading malignant melanoma of skin, Malignant melanoma, Malignant tumor of cervix, Inflammatory carcinoma of breast, Large cell carcinoma of lung, Cholangiocarcinoma, Primary malignant neoplasm of the peritoneum, Astrocytoma of brain, Superficial spreading melanoma, Carcinoma of esophagus, Klatskin's tumor, Siewert type III adenocarcinoma of esophagogastric junction, Malignant tumor of gallbladder, Primary malignant neoplasm of perihilar bile duct, Cholangiocarcinoma of biliary tract, Siewert type I adenocarcinoma of esophagogastric junction, Primary malignant clear cell tumor of ovary, Carcinosarcoma of ovary, Malignant tumor of stomach, Glioma, Squamous cell carcinoma of cervix, Endometrioid carcinoma, Nodular melanoma, Adenosquamous carcinoma of cervix, Endometrioid carcinoma ovary, Mucinous carcinoma of breast, Adenocarcinoma of stomach, or Papillary thyroid carcinoma</i></p> <p>— <i>Entrectinib in Malignant tumor of colon, Invasive micropapillary carcinoma of breast, Carcinoma of salivary gland type, Desmoplastic malignant melanoma, Endometrial carcinoma, Anaplastic thyroid carcinoma, Siewert type II adenocarcinoma of esophagogastric junction, Adenocarcinoma of cervix, Nodular malignant melanoma of skin, Adenocarcinoma of pancreas, Sarcoma of soft tissue, Adenocarcinoma of lung, Malignant tumor of vulva, Primary adenocarcinoma of colon, Malignant tumor of fallopian tube, Squamous cell carcinoma of vulva, Adenocarcinoma of rectum, Infiltrating lobular carcinoma of breast, Malignant tumor of ovary, Malignant tumor of rectum, Malignant neoplasm of endometrium of corpus uteri, Malignant tumor of thyroid gland, High grade endometrial stromal sarcoma, Mixed ductal and lobular carcinoma of breast, Non-small cell carcinoma, Hurthle cell carcinoma of thyroid, Neuroendocrine carcinoma, Malignant tumor of esophagus, Non-small cell lung cancer, Acral lentiginous malignant melanoma of skin, Adenocarcinoma of esophagus, Undifferentiated sarcoma, Malignant tumor of vagina, Infiltrating carcinoma with ductal and lobular features, Malignant tumor of salivary gland, Malignant neoplasm of uterus, Malignant melanoma of skin, Primary malignant neoplasm of cystic duct, Squamous cell carcinoma of lung, Squamous cell carcinoma of esophagus, Hepatocellular carcinoma, Malignant tumor of pancreas, Gastrointestinal stromal tumor, Malignant epithelial tumor of ovary, Lentigo maligna, Leiomyosarcoma of uterus, Malignant tumor of breast, Primary malignant neoplasm of distal bile duct, Follicular thyroid carcinoma, Malignant neoplasm of intrahepatic gall duct, Infiltrating duct carcinoma of breast, Superficial spreading malignant melanoma of skin, Malignant tumor of cervix, Inflammatory carcinoma of breast, Large cell carcinoma of lung, Cholangiocarcinoma, Primary malignant neoplasm of the peritoneum, Superficial spreading melanoma, Carcinoma of esophagus, Klatskin's tumor, Sarcoma,</i></p>

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*Siewert type III adenocarcinoma of esophagogastric junction, Malignant tumor of gallbladder, Primary malignant neoplasm of perihilar bile duct, Siewert type I adenocarcinoma of esophagogastric junction, Primary malignant clear cell tumor of ovary, Carcinosarcoma of ovary, Malignant tumor of stomach, Squamous cell carcinoma of cervix, Endometrioid carcinoma, Nodular melanoma, Adenosquamous carcinoma of cervix, Endometrioid carcinoma ovary, Adenocarcinoma of stomach, Mucinous carcinoma of breast, or Papillary thyroid carcinoma*

INTERPRETATION

(1) The FDA recently approved larotrectinib and entrectinib for treatment of patients with NTRK gene fusion-positive tumors, and the panel also recommends NTRK therapy options such as larotrectinib and entrectinib for patients with recurrent NTRK gene fusion-positive salivary gland tumors and distant metastases. (2) NTRK status should be evaluated in mammary analogue secretory carcinoma of the salivary gland. (3) Useful in certain circumstances as single-agent systemic therapy for NTRK gene fusion-positive recurrent disease with (a) distant metastases in patients with a performance status (PS) of 0-3, (b) unresectable locoregional recurrence or second primary with prior radiation therapy.

**QKI, NTRK2**

QKI-NTRK2 fusion transcript

C

**May benefit from**

- Bevacizumab-bvzr, Bevacizumab-awwb, Bevacizumab, or Atezolizumab *in Nonsquamous non-small cell neoplasm of lung, Adenocarcinoma of lung, or Large cell carcinoma of lung*
- Pembrolizumab or Ipilimumab + Nivolumab *in Squamous cell carcinoma of lung, Adenocarcinoma of lung, Non-small cell lung cancer, Large cell carcinoma of lung, or Non-small cell carcinoma*
- Larotrectinib *in Malignant tumor of colon, Malignant tumor of lung, Invasive micropapillary carcinoma of breast, Carcinoma of salivary gland type, Endometrial carcinoma, Desmoplastic malignant melanoma, Anaplastic thyroid carcinoma, Siewert type II adenocarcinoma of esophagogastric junction, Adenocarcinoma of cervix, Nodular malignant melanoma of skin, Adenocarcinoma of pancreas, Sarcoma of soft tissue, Adenocarcinoma of lung, Primary adenocarcinoma of colon, Malignant tumor of fallopian tube, Squamous cell carcinoma of vulva, Adenocarcinoma of rectum, Infiltrating lobular carcinoma of breast, Malignant tumor of ovary, Malignant tumor of rectum, Malignant tumor of thyroid gland, Infantile fibrosarcoma, Mixed ductal and lobular carcinoma of breast, High grade endometrial stromal sarcoma, Adenocarcinoma of small intestine, Non-small cell carcinoma, Hurthle cell carcinoma*

STUDY	DISEASE	PARTICIPANT	REPORT DATE	REPORT STATUS
haib20SL6185	Uncertain diagnosis	6185-SL-0046		Final

VARIANT	CLINICAL IMPACT
	<p><i>of thyroid, Malignant tumor of esophagus, Non-small cell lung cancer, Malignant tumor of appendix, Acral lentiginous malignant melanoma of skin, Adenocarcinoma of esophagus, Undifferentiated sarcoma, Infiltrating carcinoma with ductal and lobular features, Malignant tumor of salivary gland, Malignant melanoma of skin, Primary malignant neoplasm of cystic duct, Squamous cell carcinoma of lung, Squamous cell carcinoma of esophagus, Glioblastoma, Hepatocellular carcinoma, Malignant tumor of pancreas, Gastrointestinal stromal tumor, Malignant epithelial tumor of ovary, Lentigo maligna, Leiomyosarcoma of uterus, Malignant tumor of breast, Primary malignant neoplasm of distal bile duct, Infiltrating duct carcinoma of breast, Follicular thyroid carcinoma, Malignant neoplasm of intrahepatic gall duct, Superficial spreading malignant melanoma of skin, Malignant melanoma, Malignant tumor of cervix, Inflammatory carcinoma of breast, Large cell carcinoma of lung, Cholangiocarcinoma, Primary malignant neoplasm of the peritoneum, Astrocytoma of brain, Superficial spreading melanoma, Carcinoma of esophagus, Klatskin's tumor, Siewert type III adenocarcinoma of esophagogastric junction, Malignant tumor of gallbladder, Primary malignant neoplasm of perihilar bile duct, Cholangiocarcinoma of biliary tract, Siewert type I adenocarcinoma of esophagogastric junction, Primary malignant clear cell tumor of ovary, Carcinosarcoma of ovary, Malignant tumor of stomach, Glioma, Squamous cell carcinoma of cervix, Endometrioid carcinoma, Nodular melanoma, Adenosquamous carcinoma of cervix, Endometrioid carcinoma ovary, Mucinous carcinoma of breast, Adenocarcinoma of stomach, or Papillary thyroid carcinoma</i></p> <p>— Entrectinib in <i>Malignant tumor of colon, Invasive micropapillary carcinoma of breast, Carcinoma of salivary gland type, Desmoplastic malignant melanoma, Endometrial carcinoma, Anaplastic thyroid carcinoma, Siewert type II adenocarcinoma of esophagogastric junction, Adenocarcinoma of cervix, Nodular malignant melanoma of skin, Adenocarcinoma of pancreas, Sarcoma of soft tissue, Adenocarcinoma of lung, Malignant tumor of vulva, Primary adenocarcinoma of colon, Malignant tumor of fallopian tube, Squamous cell carcinoma of vulva, Adenocarcinoma of rectum, Infiltrating lobular carcinoma of breast, Malignant tumor of ovary, Malignant tumor of rectum, Malignant neoplasm of endometrium of corpus uteri, Malignant tumor of thyroid gland, High grade endometrial stromal sarcoma, Mixed ductal and lobular carcinoma of breast, Non-small cell carcinoma, Hurthle cell carcinoma of thyroid, Neuroendocrine carcinoma, Malignant tumor of esophagus, Non-small cell lung cancer, Acral lentiginous malignant melanoma of skin, Adenocarcinoma of esophagus, Undifferentiated sarcoma, Malignant tumor of vagina, Infiltrating carcinoma with ductal and lobular features, Malignant tumor of salivary gland, Malignant neoplasm of uterus, Malignant melanoma of skin, Primary malignant neoplasm of cystic duct, Squamous cell carcinoma of lung, Squamous cell carcinoma of esophagus, Hepatocellular carcinoma, Malignant tumor of pancreas, Gastrointestinal stromal</i></p>

STUDY	DISEASE	PARTICIPANT	REPORT DATE	REPORT STATUS
haib20SL6185	Uncertain diagnosis	6185-SL-0046		Final

VARIANT

CLINICAL IMPACT

*tumor, Malignant epithelial tumor of ovary, Lentigo maligna, Leiomyosarcoma of uterus, Malignant tumor of breast, Primary malignant neoplasm of distal bile duct, Follicular thyroid carcinoma, Malignant neoplasm of intrahepatic gall duct, Infiltrating duct carcinoma of breast, Superficial spreading malignant melanoma of skin, Malignant tumor of cervix, Inflammatory carcinoma of breast, Large cell carcinoma of lung, Cholangiocarcinoma, Primary malignant neoplasm of the peritoneum, Superficial spreading melanoma, Carcinoma of esophagus, Klatskin's tumor, Sarcoma, Siewert type III adenocarcinoma of esophagogastric junction, Malignant tumor of gallbladder, Primary malignant neoplasm of perihilar bile duct, Siewert type I adenocarcinoma of esophagogastric junction, Primary malignant clear cell tumor of ovary, Carcinosarcoma of ovary, Malignant tumor of stomach, Squamous cell carcinoma of cervix, Endometrioid carcinoma, Nodular melanoma, Adenosquamous carcinoma of cervix, Endometrioid carcinoma ovary, Adenocarcinoma of stomach, Mucinous carcinoma of breast, or Papillary thyroid carcinoma*

INTERPRETATION

(1) The FDA recently approved larotrectinib and entrectinib for treatment of patients with NTRK gene fusion-positive tumors, and the panel also recommends NTRK therapy options such as larotrectinib and entrectinib for patients with recurrent NTRK gene fusion-positive salivary gland tumors and distant metastases. (2) NTRK status should be evaluated in mammary analogue secretory carcinoma of the salivary gland. (3) Useful in certain circumstances as single-agent systemic therapy for NTRK gene fusion-positive recurrent disease with (a) distant metastases in patients with a performance status (PS) of 0-3, (b) unresectable locoregional recurrence or second primary with prior radiation therapy.

**TFG, NTRK1**

TFG-NTRK1 fusion transcript

C

**May benefit from**

- Bevacizumab-bvzr, Bevacizumab-awwb, Bevacizumab, or Atezolizumab *in Nonsquamous non-small cell neoplasm of lung, Adenocarcinoma of lung, or Large cell carcinoma of lung*
- Pembrolizumab or Ipilimumab + Nivolumab *in Squamous cell carcinoma of lung, Adenocarcinoma of lung, Non-small cell lung cancer, Large cell carcinoma of lung, or Non-small cell carcinoma*
- Larotrectinib *in Malignant tumor of colon, Malignant tumor of lung, Invasive micropapillary carcinoma of breast, Carcinoma of salivary gland type, Endometrial carcinoma, Desmoplastic malignant melanoma, Anaplastic thyroid carcinoma, Siewert type II adenocarcinoma of esophagogastric junction, Adenocarcinoma of cervix,*

STUDY	DISEASE	PARTICIPANT	REPORT DATE	REPORT STATUS
haib20SL6185	Uncertain diagnosis	6185-SL-0046		Final

VARIANT	CLINICAL IMPACT
	<p><i>Nodular malignant melanoma of skin, Adenocarcinoma of pancreas, Sarcoma of soft tissue, Adenocarcinoma of lung, Primary adenocarcinoma of colon, Malignant tumor of fallopian tube, Squamous cell carcinoma of vulva, Adenocarcinoma of rectum, Infiltrating lobular carcinoma of breast, Malignant tumor of ovary, Malignant tumor of rectum, Malignant tumor of thyroid gland, Infantile fibrosarcoma, Mixed ductal and lobular carcinoma of breast, High grade endometrial stromal sarcoma, Adenocarcinoma of small intestine, Non-small cell carcinoma, Hurthle cell carcinoma of thyroid, Malignant tumor of esophagus, Non-small cell lung cancer, Malignant tumor of appendix, Adenocarcinoma of esophagus, Acral lentiginous malignant melanoma of skin, Undifferentiated sarcoma, Infiltrating carcinoma with ductal and lobular features, Malignant tumor of salivary gland, Malignant melanoma of skin, Primary malignant neoplasm of cystic duct, Squamous cell carcinoma of lung, Squamous cell carcinoma of esophagus, Glioblastoma, Hepatocellular carcinoma, Malignant tumor of pancreas, Gastrointestinal stromal tumor, Malignant epithelial tumor of ovary, Lentigo maligna, Leiomyosarcoma of uterus, Malignant tumor of breast, Primary malignant neoplasm of distal bile duct, Infiltrating duct carcinoma of breast, Follicular thyroid carcinoma, Malignant neoplasm of intrahepatic gall duct, Superficial spreading malignant melanoma of skin, Malignant melanoma, Malignant tumor of cervix, Inflammatory carcinoma of breast, Large cell carcinoma of lung, Cholangiocarcinoma, Primary malignant neoplasm of the peritoneum, Astrocytoma of brain, Superficial spreading melanoma, Carcinoma of esophagus, Klatskin's tumor, Siewert type III adenocarcinoma of esophagogastric junction, Malignant tumor of gallbladder, Primary malignant neoplasm of perihilar bile duct, Cholangiocarcinoma of biliary tract, Siewert type I adenocarcinoma of esophagogastric junction, Primary malignant clear cell tumor of ovary, Carcinosarcoma of ovary, Malignant tumor of stomach, Glioma, Squamous cell carcinoma of cervix, Endometrioid carcinoma, Nodular melanoma, Adenosquamous carcinoma of cervix, Endometrioid carcinoma ovary, Mucinous carcinoma of breast, Adenocarcinoma of stomach, or Papillary thyroid carcinoma</i></p> <p>— <i>Entrectinib in Malignant tumor of colon, Invasive micropapillary carcinoma of breast, Carcinoma of salivary gland type, Desmoplastic malignant melanoma, Endometrial carcinoma, Anaplastic thyroid carcinoma, Siewert type II adenocarcinoma of esophagogastric junction, Adenocarcinoma of cervix, Nodular malignant melanoma of skin, Adenocarcinoma of pancreas, Sarcoma of soft tissue, Adenocarcinoma of lung, Malignant tumor of vulva, Primary adenocarcinoma of colon, Malignant tumor of fallopian tube, Squamous cell carcinoma of vulva, Adenocarcinoma of rectum, Infiltrating lobular carcinoma of breast, Malignant tumor of ovary, Malignant tumor of rectum, Malignant neoplasm of endometrium of corpus uteri, Malignant tumor of thyroid gland, High grade endometrial stromal sarcoma, Mixed ductal and lobular carcinoma of breast, Non-small cell carcinoma, Hurthle cell carcinoma of thyroid,</i></p>

STUDY	DISEASE	PARTICIPANT	REPORT DATE	REPORT STATUS
haib20SL6185	Uncertain diagnosis	6185-SL-0046		Final

VARIANT

CLINICAL IMPACT

*Neuroendocrine carcinoma, Malignant tumor of esophagus, Non-small cell lung cancer, Acral lentiginous malignant melanoma of skin, Adenocarcinoma of esophagus, Undifferentiated sarcoma, Malignant tumor of vagina, Infiltrating carcinoma with ductal and lobular features, Malignant tumor of salivary gland, Malignant neoplasm of uterus, Malignant melanoma of skin, Primary malignant neoplasm of cystic duct, Squamous cell carcinoma of lung, Squamous cell carcinoma of esophagus, Hepatocellular carcinoma, Malignant tumor of pancreas, Gastrointestinal stromal tumor, Malignant epithelial tumor of ovary, Lentigo maligna, Leiomyosarcoma of uterus, Malignant tumor of breast, Primary malignant neoplasm of distal bile duct, Follicular thyroid carcinoma, Malignant neoplasm of intrahepatic gall duct, Infiltrating duct carcinoma of breast, Superficial spreading malignant melanoma of skin, Malignant tumor of cervix, Inflammatory carcinoma of breast, Large cell carcinoma of lung, Cholangiocarcinoma, Primary malignant neoplasm of the peritoneum, Superficial spreading melanoma, Carcinoma of esophagus, Klatskin's tumor, Sarcoma, Siewert type III adenocarcinoma of esophagogastric junction, Malignant tumor of gallbladder, Primary malignant neoplasm of perihilar bile duct, Siewert type I adenocarcinoma of esophagogastric junction, Primary malignant clear cell tumor of ovary, Carcinosarcoma of ovary, Malignant tumor of stomach, Squamous cell carcinoma of cervix, Endometrioid carcinoma, Nodular melanoma, Adenosquamous carcinoma of cervix, Endometrioid carcinoma ovary, Adenocarcinoma of stomach, Mucinous carcinoma of breast, or Papillary thyroid carcinoma*

INTERPRETATION

(1) The FDA recently approved larotrectinib and entrectinib for treatment of patients with NTRK gene fusion-positive tumors, and the panel also recommends NTRK therapy options such as larotrectinib and entrectinib for patients with recurrent NTRK gene fusion-positive salivary gland tumors and distant metastases. (2) NTRK status should be evaluated in mammary analogue secretory carcinoma of the salivary gland. (3) Useful in certain circumstances as single-agent systemic therapy for NTRK gene fusion-positive recurrent disease with (a) distant metastases in patients with a performance status (PS) of 0-3, (b) unresectable locoregional recurrence or second primary with prior radiation therapy.

**AFAP1, NTRK2**

AFAP1-NTRK2  
fusion transcript

**May benefit from**

— Bevacizumab-bvzr, Bevacizumab-awwb, Bevacizumab, or Atezolizumab *in Nonsquamous nonsmall cell neoplasm of lung, Adenocarcinoma of lung, or Large cell carcinoma of lung*



STUDY	DISEASE	PARTICIPANT	REPORT DATE	REPORT STATUS
haib20SL6185	Uncertain diagnosis	6185-SL-0046		Final

VARIANT	CLINICAL IMPACT
C	<ul style="list-style-type: none"> <li>— Pembrolizumab or Ipilimumab + Nivolumab in Squamous cell carcinoma of lung, Adenocarcinoma of lung, Non-small cell lung cancer, Large cell carcinoma of lung, or Non-small cell carcinoma</li> <li>— Larotrectinib in Malignant tumor of colon, Malignant tumor of lung, Invasive micropapillary carcinoma of breast, Carcinoma of salivary gland type, Endometrial carcinoma, Desmoplastic malignant melanoma, Anaplastic thyroid carcinoma, Siewert type II adenocarcinoma of esophagogastric junction, Adenocarcinoma of cervix, Nodular malignant melanoma of skin, Adenocarcinoma of pancreas, Sarcoma of soft tissue, Adenocarcinoma of lung, Primary adenocarcinoma of colon, Malignant tumor of fallopian tube, Squamous cell carcinoma of vulva, Adenocarcinoma of rectum, Infiltrating lobular carcinoma of breast, Malignant tumor of ovary, Malignant tumor of rectum, Malignant tumor of thyroid gland, Infantile fibrosarcoma, Mixed ductal and lobular carcinoma of breast, High grade endometrial stromal sarcoma, Adenocarcinoma of small intestine, Non-small cell carcinoma, Hurthle cell carcinoma of thyroid, Malignant tumor of esophagus, Non-small cell lung cancer, Malignant tumor of appendix, Acral lentiginous malignant melanoma of skin, Adenocarcinoma of esophagus, Undifferentiated sarcoma, Infiltrating carcinoma with ductal and lobular features, Malignant tumor of salivary gland, Malignant melanoma of skin, Primary malignant neoplasm of cystic duct, Squamous cell carcinoma of lung, Squamous cell carcinoma of esophagus, Glioblastoma, Hepatocellular carcinoma, Malignant tumor of pancreas, Gastrointestinal stromal tumor, Malignant epithelial tumor of ovary, Lentigo maligna, Leiomyosarcoma of uterus, Malignant tumor of breast, Primary malignant neoplasm of distal bile duct, Infiltrating duct carcinoma of breast, Follicular thyroid carcinoma, Malignant neoplasm of intrahepatic gall duct, Superficial spreading malignant melanoma of skin, Malignant melanoma, Malignant tumor of cervix, Inflammatory carcinoma of breast, Large cell carcinoma of lung, Cholangiocarcinoma, Primary malignant neoplasm of the peritoneum, Astrocytoma of brain, Superficial spreading melanoma, Carcinoma of esophagus, Klatskin's tumor, Siewert type III adenocarcinoma of esophagogastric junction, Malignant tumor of gallbladder, Primary malignant neoplasm of perihilar bile duct, Cholangiocarcinoma of biliary tract, Siewert type I adenocarcinoma of esophagogastric junction, Primary malignant clear cell tumor of ovary, Carcinosarcoma of ovary, Malignant tumor of stomach, Glioma, Squamous cell carcinoma of cervix, Endometrioid carcinoma, Nodular melanoma, Adenosquamous carcinoma of cervix, Endometrioid carcinoma ovary, Mucinous carcinoma of breast, Adenocarcinoma of stomach, or Papillary thyroid carcinoma</li> <li>— Entrectinib in Malignant tumor of colon, Invasive micropapillary carcinoma of breast, Carcinoma of salivary gland type, Desmoplastic malignant melanoma, Endometrial carcinoma, Anaplastic thyroid carcinoma, Siewert type II adenocarcinoma of esophagogastric junction, Adenocarcinoma of cervix, Nodular malignant melanoma of</li> </ul>

STUDY	DISEASE	PARTICIPANT	REPORT DATE	REPORT STATUS
haib20SL6185	Uncertain diagnosis	6185-SL-0046		Final

VARIANT	CLINICAL IMPACT
	<p><i>skin, Adenocarcinoma of pancreas, Sarcoma of soft tissue, Adenocarcinoma of lung, Malignant tumor of vulva, Primary adenocarcinoma of colon, Malignant tumor of fallopian tube, Squamous cell carcinoma of vulva, Adenocarcinoma of rectum, Infiltrating lobular carcinoma of breast, Malignant tumor of ovary, Malignant tumor of rectum, Malignant neoplasm of endometrium of corpus uteri, Malignant tumor of thyroid gland, High grade endometrial stromal sarcoma, Mixed ductal and lobular carcinoma of breast, Non-small cell carcinoma, Hurthle cell carcinoma of thyroid, Neuroendocrine carcinoma, Malignant tumor of esophagus, Non-small cell lung cancer, Acral lentiginous malignant melanoma of skin, Adenocarcinoma of esophagus, Undifferentiated sarcoma, Malignant tumor of vagina, Infiltrating carcinoma with ductal and lobular features, Malignant tumor of salivary gland, Malignant neoplasm of uterus, Malignant melanoma of skin, Primary malignant neoplasm of cystic duct, Squamous cell carcinoma of lung, Squamous cell carcinoma of esophagus, Hepatocellular carcinoma, Malignant tumor of pancreas, Gastrointestinal stromal tumor, Malignant epithelial tumor of ovary, Lentigo maligna, Leiomyosarcoma of uterus, Malignant tumor of breast, Primary malignant neoplasm of distal bile duct, Follicular thyroid carcinoma, Malignant neoplasm of intrahepatic gall duct, Infiltrating duct carcinoma of breast, Superficial spreading malignant melanoma of skin, Malignant tumor of cervix, Inflammatory carcinoma of breast, Large cell carcinoma of lung, Cholangiocarcinoma, Primary malignant neoplasm of the peritoneum, Superficial spreading melanoma, Carcinoma of esophagus, Klatskin's tumor, Sarcoma, Siewert type III adenocarcinoma of esophagogastric junction, Malignant tumor of gallbladder, Primary malignant neoplasm of perihilar bile duct, Siewert type I adenocarcinoma of esophagogastric junction, Primary malignant clear cell tumor of ovary, Carcinosarcoma of ovary, Malignant tumor of stomach, Squamous cell carcinoma of cervix, Endometrioid carcinoma, Nodular melanoma, Adenosquamous carcinoma of cervix, Endometrioid carcinoma ovary, Adenocarcinoma of stomach, Mucinous carcinoma of breast, or Papillary thyroid carcinoma</i></p>

INTERPRETATION

(1) The FDA recently approved larotrectinib and entrectinib for treatment of patients with NTRK gene fusion-positive tumors, and the panel also recommends NTRK therapy options such as larotrectinib and entrectinib for patients with recurrent NTRK gene fusion-positive salivary gland tumors and distant metastases. (2) NTRK status should be evaluated in mammary analogue secretory carcinoma of the salivary gland. (3) Useful in certain circumstances as single-agent systemic therapy for NTRK gene fusion-positive recurrent disease with (a) distant metastases in

STUDY	DISEASE	PARTICIPANT	REPORT DATE	REPORT STATUS
haib20SL6185	Uncertain diagnosis	6185-SL-0046		Final

VARIANT	CLINICAL IMPACT
	<p>INTERPRETATION</p> <p>patients with a performance status (PS) of 0-3, (b) unresectable locoregional recurrence or second primary with prior radiation therapy.</p>

**BTBD1, NTRK3**

BTBD1-NTRK3  
fusion transcript

C

**May benefit from**

- Bevacizumab-bvzr, Bevacizumab-awwb, Bevacizumab, or Atezolizumab in *Nonsquamous nonsmall cell neoplasm of lung, Adenocarcinoma of lung, or Large cell carcinoma of lung*
- Pembrolizumab or Ipilimumab + Nivolumab in *Squamous cell carcinoma of lung, Adenocarcinoma of lung, Non-small cell lung cancer, Large cell carcinoma of lung, or Non-small cell carcinoma*
- Larotrectinib in *Malignant tumor of colon, Malignant tumor of lung, Invasive micropapillary carcinoma of breast, Carcinoma of salivary gland type, Desmoplastic malignant melanoma, Endometrial carcinoma, Anaplastic thyroid carcinoma, Siewert type II adenocarcinoma of esophagogastric junction, Adenocarcinoma of cervix, Nodular malignant melanoma of skin, Adenocarcinoma of pancreas, Sarcoma of soft tissue, Adenocarcinoma of lung, Primary adenocarcinoma of colon, Malignant tumor of fallopian tube, Squamous cell carcinoma of vulva, Adenocarcinoma of rectum, Infiltrating lobular carcinoma of breast, Malignant tumor of ovary, Malignant tumor of rectum, Malignant tumor of thyroid gland, Infantile fibrosarcoma, Mixed ductal and lobular carcinoma of breast, High grade endometrial stromal sarcoma, Adenocarcinoma of small intestine, Non-small cell carcinoma, Hurthle cell carcinoma of thyroid, Malignant tumor of esophagus, Non-small cell lung cancer, Malignant tumor of appendix, Acral lentiginous malignant melanoma of skin, Adenocarcinoma of esophagus, Undifferentiated sarcoma, Infiltrating carcinoma with ductal and lobular features, Malignant tumor of salivary gland, Malignant melanoma of skin, Primary malignant neoplasm of cystic duct, Squamous cell carcinoma of lung, Squamous cell carcinoma of esophagus, Glioblastoma, Hepatocellular carcinoma, Malignant tumor of pancreas, Gastrointestinal stromal tumor, Malignant epithelial tumor of ovary, Lentigo maligna, Leiomyosarcoma of uterus, Malignant tumor of breast, Primary malignant neoplasm of distal bile duct, Infiltrating duct carcinoma of breast, Follicular thyroid carcinoma, Malignant neoplasm of intrahepatic gall duct, Superficial spreading malignant melanoma of skin, Malignant melanoma, Malignant tumor of cervix, Inflammatory carcinoma of breast, Large cell carcinoma of lung, Cholangiocarcinoma, Primary malignant neoplasm of the peritoneum, Astrocytoma of brain, Superficial spreading melanoma, Carcinoma of esophagus, Klatskin's tumor, Siewert type III adenocarcinoma of esophagogastric junction, Malignant tumor of gallbladder, Primary malignant neoplasm of perihilar bile duct, Cholangiocarcinoma of biliary*

STUDY	DISEASE	PARTICIPANT	REPORT DATE	REPORT STATUS
haib20SL6185	Uncertain diagnosis	6185-SL-0046		Final

VARIANT	CLINICAL IMPACT
	<p><i>tract, Siewert type I adenocarcinoma of esophagogastric junction, Primary malignant clear cell tumor of ovary, Carcinosarcoma of ovary, Malignant tumor of stomach, Glioma, Squamous cell carcinoma of cervix, Endometrioid carcinoma, Nodular melanoma, Adenosquamous carcinoma of cervix, Endometrioid carcinoma ovary, Mucinous carcinoma of breast, Adenocarcinoma of stomach, or Papillary thyroid carcinoma</i></p> <p>— <i>Entrectinib in Malignant tumor of colon, Invasive micropapillary carcinoma of breast, Carcinoma of salivary gland type, Desmoplastic malignant melanoma, Endometrial carcinoma, Anaplastic thyroid carcinoma, Siewert type II adenocarcinoma of esophagogastric junction, Adenocarcinoma of cervix, Nodular malignant melanoma of skin, Adenocarcinoma of pancreas, Sarcoma of soft tissue, Adenocarcinoma of lung, Malignant tumor of vulva, Primary adenocarcinoma of colon, Malignant tumor of fallopian tube, Squamous cell carcinoma of vulva, Adenocarcinoma of rectum, Infiltrating lobular carcinoma of breast, Malignant tumor of ovary, Malignant tumor of rectum, Malignant neoplasm of endometrium of corpus uteri, Malignant tumor of thyroid gland, High grade endometrial stromal sarcoma, Mixed ductal and lobular carcinoma of breast, Non-small cell carcinoma, Hurthle cell carcinoma of thyroid, Neuroendocrine carcinoma, Malignant tumor of esophagus, Non-small cell lung cancer, Acral lentiginous malignant melanoma of skin, Adenocarcinoma of esophagus, Undifferentiated sarcoma, Malignant tumor of vagina, Infiltrating carcinoma with ductal and lobular features, Malignant tumor of salivary gland, Malignant melanoma of skin, Malignant neoplasm of uterus, Primary malignant neoplasm of cystic duct, Squamous cell carcinoma of lung, Squamous cell carcinoma of esophagus, Hepatocellular carcinoma, Malignant tumor of pancreas, Gastrointestinal stromal tumor, Malignant epithelial tumor of ovary, Lentigo maligna, Leiomyosarcoma of uterus, Malignant tumor of breast, Primary malignant neoplasm of distal bile duct, Follicular thyroid carcinoma, Malignant neoplasm of intrahepatic gall duct, Infiltrating duct carcinoma of breast, Superficial spreading malignant melanoma of skin, Malignant tumor of cervix, Inflammatory carcinoma of breast, Large cell carcinoma of lung, Cholangiocarcinoma, Primary malignant neoplasm of the peritoneum, Superficial spreading melanoma, Carcinoma of esophagus, Klatskin's tumor, Sarcoma, Siewert type III adenocarcinoma of esophagogastric junction, Malignant tumor of gallbladder, Primary malignant neoplasm of perihilar bile duct, Siewert type I adenocarcinoma of esophagogastric junction, Primary malignant clear cell tumor of ovary, Carcinosarcoma of ovary, Malignant tumor of stomach, Squamous cell carcinoma of cervix, Endometrioid carcinoma, Nodular melanoma, Adenosquamous carcinoma of cervix, Endometrioid carcinoma ovary, Adenocarcinoma of stomach, Mucinous carcinoma of breast, or Papillary thyroid carcinoma</i></p>

STUDY	DISEASE	PARTICIPANT	REPORT DATE	REPORT STATUS
haib20SL6185	Uncertain diagnosis	6185-SL-0046		Final

VARIANT	CLINICAL IMPACT
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INTERPRETATION

(1) The FDA recently approved larotrectinib and entrectinib for treatment of patients with NTRK gene fusion-positive tumors, and the panel also recommends NTRK therapy options such as larotrectinib and entrectinib for patients with recurrent NTRK gene fusion-positive salivary gland tumors and distant metastases. (2) NTRK status should be evaluated in mammary analogue secretory carcinoma of the salivary gland. (3) Useful in certain circumstances as systemic therapy for NTRK gene fusion-positive recurrent disease with (a) distant metastases in patients with a performance status (PS) of 0-3, (b) unresectable locoregional recurrence or second primary with prior radiation therapy.

**PAN3, NTRK2**

PAN3-NTRK2 fusion transcript

C

**May benefit from**

- Bevacizumab-bvzr, Bevacizumab-awwb, Bevacizumab, or Atezolizumab *in Nonsquamous non-small cell neoplasm of lung, Adenocarcinoma of lung, or Large cell carcinoma of lung*
- Pembrolizumab or Ipilimumab + Nivolumab *in Squamous cell carcinoma of lung, Adenocarcinoma of lung, Non-small cell lung cancer, Large cell carcinoma of lung, or Non-small cell carcinoma*
- Larotrectinib *in Malignant tumor of colon, Malignant tumor of lung, Invasive micropapillary carcinoma of breast, Carcinoma of salivary gland type, Endometrial carcinoma, Desmoplastic malignant melanoma, Anaplastic thyroid carcinoma, Siewert type II adenocarcinoma of esophagogastric junction, Adenocarcinoma of cervix, Nodular malignant melanoma of skin, Adenocarcinoma of pancreas, Sarcoma of soft tissue, Adenocarcinoma of lung, Primary adenocarcinoma of colon, Malignant tumor of fallopian tube, Squamous cell carcinoma of vulva, Adenocarcinoma of rectum, Infiltrating lobular carcinoma of breast, Malignant tumor of ovary, Malignant tumor of rectum, Malignant tumor of thyroid gland, Infantile fibrosarcoma, Mixed ductal and lobular carcinoma of breast, High grade endometrial stromal sarcoma, Adenocarcinoma of small intestine, Non-small cell carcinoma, Hurthle cell carcinoma of thyroid, Malignant tumor of esophagus, Non-small cell lung cancer, Malignant tumor of appendix, Acral lentiginous malignant melanoma of skin, Adenocarcinoma of esophagus, Undifferentiated sarcoma, Infiltrating carcinoma with ductal and lobular features, Malignant tumor of salivary gland, Malignant melanoma of skin, Primary malignant neoplasm of cystic duct, Squamous cell carcinoma of lung, Squamous cell carcinoma of esophagus, Glioblastoma, Hepatocellular carcinoma, Malignant tumor of pancreas, Gastrointestinal stromal tumor, Malignant epithelial tumor of ovary, Lentigo*

STUDY	DISEASE	PARTICIPANT	REPORT DATE	REPORT STATUS
haib20SL6185	Uncertain diagnosis	6185-SL-0046		Final

VARIANT	CLINICAL IMPACT
	<p><i>maligna, Leiomyosarcoma of uterus, Malignant tumor of breast, Primary malignant neoplasm of distal bile duct, Infiltrating duct carcinoma of breast, Follicular thyroid carcinoma, Malignant neoplasm of intrahepatic gall duct, Superficial spreading malignant melanoma of skin, Malignant melanoma, Malignant tumor of cervix, Inflammatory carcinoma of breast, Large cell carcinoma of lung, Cholangiocarcinoma, Primary malignant neoplasm of the peritoneum, Astrocytoma of brain, Superficial spreading melanoma, Carcinoma of esophagus, Klatskin's tumor, Siewert type III adenocarcinoma of esophagogastric junction, Malignant tumor of gallbladder, Primary malignant neoplasm of perihilar bile duct, Cholangiocarcinoma of biliary tract, Siewert type I adenocarcinoma of esophagogastric junction, Primary malignant clear cell tumor of ovary, Carcinosarcoma of ovary, Malignant tumor of stomach, Glioma, Squamous cell carcinoma of cervix, Endometrioid carcinoma, Nodular melanoma, Adenosquamous carcinoma of cervix, Endometrioid carcinoma ovary, Mucinous carcinoma of breast, Adenocarcinoma of stomach, or Papillary thyroid carcinoma</i></p> <p>— <i>Entrectinib in Malignant tumor of colon, Invasive micropapillary carcinoma of breast, Carcinoma of salivary gland type, Desmoplastic malignant melanoma, Endometrial carcinoma, Anaplastic thyroid carcinoma, Siewert type II adenocarcinoma of esophagogastric junction, Adenocarcinoma of cervix, Nodular malignant melanoma of skin, Adenocarcinoma of pancreas, Sarcoma of soft tissue, Adenocarcinoma of lung, Malignant tumor of vulva, Primary adenocarcinoma of colon, Malignant tumor of fallopian tube, Squamous cell carcinoma of vulva, Adenocarcinoma of rectum, Infiltrating lobular carcinoma of breast, Malignant tumor of ovary, Malignant tumor of rectum, Malignant neoplasm of endometrium of corpus uteri, Malignant tumor of thyroid gland, High grade endometrial stromal sarcoma, Mixed ductal and lobular carcinoma of breast, Non-small cell carcinoma, Hurthle cell carcinoma of thyroid, Neuroendocrine carcinoma, Malignant tumor of esophagus, Non-small cell lung cancer, Acral lentiginous malignant melanoma of skin, Adenocarcinoma of esophagus, Undifferentiated sarcoma, Malignant tumor of vagina, Infiltrating carcinoma with ductal and lobular features, Malignant tumor of salivary gland, Malignant neoplasm of uterus, Malignant melanoma of skin, Primary malignant neoplasm of cystic duct, Squamous cell carcinoma of lung, Squamous cell carcinoma of esophagus, Hepatocellular carcinoma, Malignant tumor of pancreas, Gastrointestinal stromal tumor, Malignant epithelial tumor of ovary, Lentigo maligna, Leiomyosarcoma of uterus, Malignant tumor of breast, Primary malignant neoplasm of distal bile duct, Follicular thyroid carcinoma, Malignant neoplasm of intrahepatic gall duct, Infiltrating duct carcinoma of breast, Superficial spreading malignant melanoma of skin, Malignant tumor of cervix, Inflammatory carcinoma of breast, Large cell carcinoma of lung, Cholangiocarcinoma, Primary malignant neoplasm of the peritoneum, Superficial spreading melanoma, Carcinoma of esophagus, Klatskin's tumor, Sarcoma,</i></p>

STUDY	DISEASE	PARTICIPANT	REPORT DATE	REPORT STATUS
haib20SL6185	Uncertain diagnosis	6185-SL-0046		Final

VARIANT

CLINICAL IMPACT

*Siewert type III adenocarcinoma of esophagogastric junction, Malignant tumor of gallbladder, Primary malignant neoplasm of perihilar bile duct, Siewert type I adenocarcinoma of esophagogastric junction, Primary malignant clear cell tumor of ovary, Carcinosarcoma of ovary, Malignant tumor of stomach, Squamous cell carcinoma of cervix, Endometrioid carcinoma, Nodular melanoma, Adenosquamous carcinoma of cervix, Endometrioid carcinoma ovary, Adenocarcinoma of stomach, Mucinous carcinoma of breast, or Papillary thyroid carcinoma*

INTERPRETATION

(1) The FDA recently approved larotrectinib and entrectinib for treatment of patients with NTRK gene fusion-positive tumors, and the panel also recommends NTRK therapy options such as larotrectinib and entrectinib for patients with recurrent NTRK gene fusion-positive salivary gland tumors and distant metastases. (2) NTRK status should be evaluated in mammary analogue secretory carcinoma of the salivary gland. (3) Useful in certain circumstances as single-agent systemic therapy for NTRK gene fusion-positive recurrent disease with (a) distant metastases in patients with a performance status (PS) of 0-3, (b) unresectable locoregional recurrence or second primary with prior radiation therapy.

**ETV6, NTRK3**

ETV6-NTRK3 fusion transcript

C

**May benefit from**

- Bevacizumab-bvzr, Bevacizumab-awwb, Bevacizumab, or Atezolizumab *in Nonsquamous non-small cell neoplasm of lung, Adenocarcinoma of lung, or Large cell carcinoma of lung*
- Pembrolizumab or Ipilimumab + Nivolumab *in Squamous cell carcinoma of lung, Adenocarcinoma of lung, Non-small cell lung cancer, Large cell carcinoma of lung, or Non-small cell carcinoma*
- Larotrectinib *in Malignant tumor of colon, Malignant tumor of lung, Invasive micropapillary carcinoma of breast, Carcinoma of salivary gland type, Desmoplastic malignant melanoma, Endometrial carcinoma, Anaplastic thyroid carcinoma, Siewert type II adenocarcinoma of esophagogastric junction, Adenocarcinoma of cervix, Nodular malignant melanoma of skin, Adenocarcinoma of pancreas, Sarcoma of soft tissue, Adenocarcinoma of lung, Primary adenocarcinoma of colon, Malignant tumor of fallopian tube, Squamous cell carcinoma of vulva, Adenocarcinoma of rectum, Infiltrating lobular carcinoma of breast, Malignant tumor of ovary, Malignant tumor of rectum, Malignant tumor of thyroid gland, Infantile fibrosarcoma, Mixed ductal and lobular carcinoma of breast, High grade endometrial stromal sarcoma, Adenocarcinoma of small intestine, Non-small cell carcinoma, Hurthle cell carcinoma*

STUDY	DISEASE	PARTICIPANT	REPORT DATE	REPORT STATUS
haib20SL6185	Uncertain diagnosis	6185-SL-0046		Final

VARIANT	CLINICAL IMPACT
	<p><i>of thyroid, Malignant tumor of esophagus, Non-small cell lung cancer, Malignant tumor of appendix, Acral lentiginous malignant melanoma of skin, Adenocarcinoma of esophagus, Undifferentiated sarcoma, Infiltrating carcinoma with ductal and lobular features, Malignant tumor of salivary gland, Malignant melanoma of skin, Primary malignant neoplasm of cystic duct, Squamous cell carcinoma of lung, Squamous cell carcinoma of esophagus, Glioblastoma, Hepatocellular carcinoma, Malignant tumor of pancreas, Gastrointestinal stromal tumor, Malignant epithelial tumor of ovary, Lentigo maligna, Leiomyosarcoma of uterus, Malignant tumor of breast, Primary malignant neoplasm of distal bile duct, Infiltrating duct carcinoma of breast, Follicular thyroid carcinoma, Malignant neoplasm of intrahepatic gall duct, Superficial spreading malignant melanoma of skin, Malignant melanoma, Malignant tumor of cervix, Inflammatory carcinoma of breast, Large cell carcinoma of lung, Cholangiocarcinoma, Primary malignant neoplasm of the peritoneum, Astrocytoma of brain, Superficial spreading melanoma, Carcinoma of esophagus, Klatskin's tumor, Siewert type III adenocarcinoma of esophagogastric junction, Malignant tumor of gallbladder, Primary malignant neoplasm of perihilar bile duct, Cholangiocarcinoma of biliary tract, Siewert type I adenocarcinoma of esophagogastric junction, Primary malignant clear cell tumor of ovary, Carcinosarcoma of ovary, Malignant tumor of stomach, Glioma, Squamous cell carcinoma of cervix, Endometrioid carcinoma, Nodular melanoma, Adenosquamous carcinoma of cervix, Endometrioid carcinoma ovary, Mucinous carcinoma of breast, Adenocarcinoma of stomach, or Papillary thyroid carcinoma</i></p> <p>— Entrectinib in <i>Malignant tumor of colon, Invasive micropapillary carcinoma of breast, Carcinoma of salivary gland type, Desmoplastic malignant melanoma, Endometrial carcinoma, Anaplastic thyroid carcinoma, Siewert type II adenocarcinoma of esophagogastric junction, Adenocarcinoma of cervix, Nodular malignant melanoma of skin, Adenocarcinoma of pancreas, Sarcoma of soft tissue, Adenocarcinoma of lung, Malignant tumor of vulva, Primary adenocarcinoma of colon, Malignant tumor of fallopian tube, Squamous cell carcinoma of vulva, Adenocarcinoma of rectum, Infiltrating lobular carcinoma of breast, Malignant tumor of ovary, Malignant tumor of rectum, Malignant neoplasm of endometrium of corpus uteri, Malignant tumor of thyroid gland, High grade endometrial stromal sarcoma, Mixed ductal and lobular carcinoma of breast, Non-small cell carcinoma, Hurthle cell carcinoma of thyroid, Neuroendocrine carcinoma, Malignant tumor of esophagus, Non-small cell lung cancer, Acral lentiginous malignant melanoma of skin, Adenocarcinoma of esophagus, Undifferentiated sarcoma, Malignant tumor of vagina, Infiltrating carcinoma with ductal and lobular features, Malignant tumor of salivary gland, Malignant melanoma of skin, Malignant neoplasm of uterus, Primary malignant neoplasm of cystic duct, Squamous cell carcinoma of lung, Squamous cell carcinoma of esophagus, Hepatocellular carcinoma, Malignant tumor of pancreas, Gastrointestinal stromal</i></p>



STUDY	DISEASE	PARTICIPANT	REPORT DATE	REPORT STATUS
haib20SL6185	Uncertain diagnosis	6185-SL-0046		Final

VARIANT

CLINICAL IMPACT

*tumor, Malignant epithelial tumor of ovary, Lentigo maligna, Leiomyosarcoma of uterus, Malignant tumor of breast, Primary malignant neoplasm of distal bile duct, Follicular thyroid carcinoma, Malignant neoplasm of intrahepatic gall duct, Infiltrating duct carcinoma of breast, Superficial spreading malignant melanoma of skin, Malignant tumor of cervix, Inflammatory carcinoma of breast, Large cell carcinoma of lung, Cholangiocarcinoma, Primary malignant neoplasm of the peritoneum, Superficial spreading melanoma, Carcinoma of esophagus, Klatskin's tumor, Sarcoma, Siewert type III adenocarcinoma of esophagogastric junction, Malignant tumor of gallbladder, Primary malignant neoplasm of perihilar bile duct, Siewert type I adenocarcinoma of esophagogastric junction, Primary malignant clear cell tumor of ovary, Carcinosarcoma of ovary, Malignant tumor of stomach, Squamous cell carcinoma of cervix, Endometrioid carcinoma, Nodular melanoma, Adenosquamous carcinoma of cervix, Endometrioid carcinoma ovary, Adenocarcinoma of stomach, Mucinous carcinoma of breast, or Papillary thyroid carcinoma*

**Diagnostic of**

- Infantile fibrosarcoma

INTERPRETATION

(1) The FDA recently approved larotrectinib and entrectinib for treatment of patients with NTRK gene fusion-positive tumors, and the panel also recommends NTRK therapy options such as larotrectinib and entrectinib for patients with recurrent NTRK gene fusion-positive salivary gland tumors and distant metastases. (2) NTRK status should be evaluated in mammary analogue secretory carcinoma of the salivary gland. (3) Useful in certain circumstances as systemic therapy for NTRK gene fusion-positive recurrent disease with (a) distant metastases in patients with a performance status (PS) of 0-3, (b) unresectable locoregional recurrence or second primary with prior radiation therapy.

**ETV6, NTRK3**

ETV6-NTRK3 fusion transcript

C

**May benefit from**

- Bevacizumab-bvzr, Bevacizumab-awwb, Bevacizumab, or Atezolizumab *in Nonsquamous nonsmall cell neoplasm of lung, Adenocarcinoma of lung, or Large cell carcinoma of lung*
- Pembrolizumab or Ipilimumab + Nivolumab *in Squamous cell carcinoma of lung, Adenocarcinoma of lung, Non-small cell lung cancer, Large cell carcinoma of lung, or Non-small cell carcinoma*

STUDY	DISEASE	PARTICIPANT	REPORT DATE	REPORT STATUS
haib20SL6185	Uncertain diagnosis	6185-SL-0046		Final

VARIANT

CLINICAL IMPACT

- Larotrectinib in *Malignant tumor of colon, Malignant tumor of lung, Invasive micropapillary carcinoma of breast, Carcinoma of salivary gland type, Desmoplastic malignant melanoma, Endometrial carcinoma, Anaplastic thyroid carcinoma, Siewert type II adenocarcinoma of esophagogastric junction, Adenocarcinoma of cervix, Nodular malignant melanoma of skin, Adenocarcinoma of pancreas, Sarcoma of soft tissue, Adenocarcinoma of lung, Primary adenocarcinoma of colon, Malignant tumor of fallopian tube, Squamous cell carcinoma of vulva, Adenocarcinoma of rectum, Infiltrating lobular carcinoma of breast, Malignant tumor of ovary, Malignant tumor of rectum, Malignant tumor of thyroid gland, Infantile fibrosarcoma, Mixed ductal and lobular carcinoma of breast, High grade endometrial stromal sarcoma, Adenocarcinoma of small intestine, Non-small cell carcinoma, Hurthle cell carcinoma of thyroid, Malignant tumor of esophagus, Non-small cell lung cancer, Malignant tumor of appendix, Acral lentiginous malignant melanoma of skin, Adenocarcinoma of esophagus, Undifferentiated sarcoma, Infiltrating carcinoma with ductal and lobular features, Malignant tumor of salivary gland, Malignant melanoma of skin, Primary malignant neoplasm of cystic duct, Squamous cell carcinoma of lung, Squamous cell carcinoma of esophagus, Glioblastoma, Hepatocellular carcinoma, Malignant tumor of pancreas, Gastrointestinal stromal tumor, Malignant epithelial tumor of ovary, Lentigo maligna, Leiomyosarcoma of uterus, Malignant tumor of breast, Primary malignant neoplasm of distal bile duct, Infiltrating duct carcinoma of breast, Follicular thyroid carcinoma, Malignant neoplasm of intrahepatic gall duct, Superficial spreading malignant melanoma of skin, Malignant melanoma, Malignant tumor of cervix, Inflammatory carcinoma of breast, Large cell carcinoma of lung, Cholangiocarcinoma, Primary malignant neoplasm of the peritoneum, Astrocytoma of brain, Superficial spreading melanoma, Carcinoma of esophagus, Klatskin's tumor, Siewert type III adenocarcinoma of esophagogastric junction, Malignant tumor of gallbladder, Primary malignant neoplasm of perihilar bile duct, Cholangiocarcinoma of biliary tract, Siewert type I adenocarcinoma of esophagogastric junction, Primary malignant clear cell tumor of ovary, Carcinosarcoma of ovary, Malignant tumor of stomach, Glioma, Squamous cell carcinoma of cervix, Endometrioid carcinoma, Nodular melanoma, Adenosquamous carcinoma of cervix, Endometrioid carcinoma ovary, Mucinous carcinoma of breast, Adenocarcinoma of stomach, or Papillary thyroid carcinoma*
- Entrectinib in *Malignant tumor of colon, Invasive micropapillary carcinoma of breast, Carcinoma of salivary gland type, Desmoplastic malignant melanoma, Endometrial carcinoma, Anaplastic thyroid carcinoma, Siewert type II adenocarcinoma of esophagogastric junction, Adenocarcinoma of cervix, Nodular malignant melanoma of skin, Adenocarcinoma of pancreas, Sarcoma of soft tissue, Adenocarcinoma of lung, Malignant tumor of vulva, Primary adenocarcinoma of colon, Malignant tumor of fallopian tube, Squamous cell carcinoma of vulva, Adenocarcinoma of rectum,*

STUDY	DISEASE	PARTICIPANT	REPORT DATE	REPORT STATUS
haib20SL6185	Uncertain diagnosis	6185-SL-0046		Final

VARIANT

CLINICAL IMPACT

*Infiltrating lobular carcinoma of breast, Malignant tumor of ovary, Malignant tumor of rectum, Malignant neoplasm of endometrium of corpus uteri, Malignant tumor of thyroid gland, High grade endometrial stromal sarcoma, Mixed ductal and lobular carcinoma of breast, Non-small cell carcinoma, Hurthle cell carcinoma of thyroid, Neuroendocrine carcinoma, Malignant tumor of esophagus, Non-small cell lung cancer, Acral lentiginous malignant melanoma of skin, Adenocarcinoma of esophagus, Undifferentiated sarcoma, Malignant tumor of vagina, Infiltrating carcinoma with ductal and lobular features, Malignant tumor of salivary gland, Malignant melanoma of skin, Malignant neoplasm of uterus, Primary malignant neoplasm of cystic duct, Squamous cell carcinoma of lung, Squamous cell carcinoma of esophagus, Hepatocellular carcinoma, Malignant tumor of pancreas, Gastrointestinal stromal tumor, Malignant epithelial tumor of ovary, Lentigo maligna, Leiomyosarcoma of uterus, Malignant tumor of breast, Primary malignant neoplasm of distal bile duct, Follicular thyroid carcinoma, Malignant neoplasm of intrahepatic gall duct, Infiltrating duct carcinoma of breast, Superficial spreading malignant melanoma of skin, Malignant tumor of cervix, Inflammatory carcinoma of breast, Large cell carcinoma of lung, Cholangiocarcinoma, Primary malignant neoplasm of the peritoneum, Superficial spreading melanoma, Carcinoma of esophagus, Klatskin's tumor, Sarcoma, Siewert type III adenocarcinoma of esophagogastric junction, Malignant tumor of gallbladder, Primary malignant neoplasm of perihilar bile duct, Siewert type I adenocarcinoma of esophagogastric junction, Primary malignant clear cell tumor of ovary, Carcinosarcoma of ovary, Malignant tumor of stomach, Squamous cell carcinoma of cervix, Endometrioid carcinoma, Nodular melanoma, Adenosquamous carcinoma of cervix, Endometrioid carcinoma ovary, Adenocarcinoma of stomach, Mucinous carcinoma of breast, or Papillary thyroid carcinoma*

**Diagnostic of**

- Infantile fibrosarcoma

INTERPRETATION

(1) The FDA recently approved larotrectinib and entrectinib for treatment of patients with NTRK gene fusion-positive tumors, and the panel also recommends NTRK therapy options such as larotrectinib and entrectinib for patients with recurrent NTRK gene fusion-positive salivary gland tumors and distant metastases. (2) NTRK status should be evaluated in mammary analogue secretory carcinoma of the salivary gland. (3) Useful in certain circumstances as systemic therapy for NTRK gene fusion-positive recurrent disease with (a) distant metastases in patients with a

STUDY	DISEASE	PARTICIPANT	REPORT DATE	REPORT STATUS
haib20SL6185	Uncertain diagnosis	6185-SL-0046		Final

VARIANT

CLINICAL IMPACT

INTERPRETATION

performance status (PS) of 0-3, (b) unresectable locoregional recurrence or second primary with prior radiation therapy.

**ETV6, NTRK3**

ETV6-NTRK3 fusion transcript

C

**May benefit from**

- Bevacizumab-bvzr, Bevacizumab-awwb, Bevacizumab, or Atezolizumab in *Nonsquamous nonsmall cell neoplasm of lung, Adenocarcinoma of lung, or Large cell carcinoma of lung*
- Pembrolizumab or Ipilimumab + Nivolumab in *Squamous cell carcinoma of lung, Adenocarcinoma of lung, Non-small cell lung cancer, Large cell carcinoma of lung, or Non-small cell carcinoma*
- Larotrectinib in *Malignant tumor of colon, Malignant tumor of lung, Invasive micropapillary carcinoma of breast, Carcinoma of salivary gland type, Desmoplastic malignant melanoma, Endometrial carcinoma, Anaplastic thyroid carcinoma, Siewert type II adenocarcinoma of esophagogastric junction, Adenocarcinoma of cervix, Nodular malignant melanoma of skin, Adenocarcinoma of pancreas, Sarcoma of soft tissue, Adenocarcinoma of lung, Primary adenocarcinoma of colon, Malignant tumor of fallopian tube, Squamous cell carcinoma of vulva, Adenocarcinoma of rectum, Infiltrating lobular carcinoma of breast, Malignant tumor of ovary, Malignant tumor of rectum, Malignant tumor of thyroid gland, Infantile fibrosarcoma, Mixed ductal and lobular carcinoma of breast, High grade endometrial stromal sarcoma, Adenocarcinoma of small intestine, Non-small cell carcinoma, Hurthle cell carcinoma of thyroid, Malignant tumor of esophagus, Non-small cell lung cancer, Malignant tumor of appendix, Acral lentiginous malignant melanoma of skin, Adenocarcinoma of esophagus, Undifferentiated sarcoma, Infiltrating carcinoma with ductal and lobular features, Malignant tumor of salivary gland, Malignant melanoma of skin, Primary malignant neoplasm of cystic duct, Squamous cell carcinoma of lung, Squamous cell carcinoma of esophagus, Glioblastoma, Hepatocellular carcinoma, Malignant tumor of pancreas, Gastrointestinal stromal tumor, Malignant epithelial tumor of ovary, Lentigo maligna, Leiomyosarcoma of uterus, Malignant tumor of breast, Primary malignant neoplasm of distal bile duct, Infiltrating duct carcinoma of breast, Follicular thyroid carcinoma, Malignant neoplasm of intrahepatic gall duct, Superficial spreading malignant melanoma of skin, Malignant melanoma, Malignant tumor of cervix, Inflammatory carcinoma of breast, Large cell carcinoma of lung, Cholangiocarcinoma, Primary malignant neoplasm of the peritoneum, Astrocytoma of brain, Superficial spreading melanoma, Carcinoma of esophagus, Klatskin's tumor, Siewert type III adenocarcinoma of esophagogastric junction, Malignant tumor of gallbladder, Primary malignant neoplasm of perihilar bile duct, Cholangiocarcinoma of biliary*

STUDY	DISEASE	PARTICIPANT	REPORT DATE	REPORT STATUS
haib20SL6185	Uncertain diagnosis	6185-SL-0046		Final

VARIANT	CLINICAL IMPACT
	<p><i>tract, Siewert type I adenocarcinoma of esophagogastric junction, Primary malignant clear cell tumor of ovary, Carcinosarcoma of ovary, Malignant tumor of stomach, Glioma, Squamous cell carcinoma of cervix, Endometrioid carcinoma, Nodular melanoma, Adenosquamous carcinoma of cervix, Endometrioid carcinoma ovary, Mucinous carcinoma of breast, Adenocarcinoma of stomach, or Papillary thyroid carcinoma</i></p> <p>— <i>Entrectinib in Malignant tumor of colon, Invasive micropapillary carcinoma of breast, Carcinoma of salivary gland type, Desmoplastic malignant melanoma, Endometrial carcinoma, Anaplastic thyroid carcinoma, Siewert type II adenocarcinoma of esophagogastric junction, Adenocarcinoma of cervix, Nodular malignant melanoma of skin, Adenocarcinoma of pancreas, Sarcoma of soft tissue, Adenocarcinoma of lung, Malignant tumor of vulva, Primary adenocarcinoma of colon, Malignant tumor of fallopian tube, Squamous cell carcinoma of vulva, Adenocarcinoma of rectum, Infiltrating lobular carcinoma of breast, Malignant tumor of ovary, Malignant tumor of rectum, Malignant neoplasm of endometrium of corpus uteri, Malignant tumor of thyroid gland, High grade endometrial stromal sarcoma, Mixed ductal and lobular carcinoma of breast, Non-small cell carcinoma, Hurthle cell carcinoma of thyroid, Neuroendocrine carcinoma, Malignant tumor of esophagus, Non-small cell lung cancer, Acral lentiginous malignant melanoma of skin, Adenocarcinoma of esophagus, Undifferentiated sarcoma, Malignant tumor of vagina, Infiltrating carcinoma with ductal and lobular features, Malignant tumor of salivary gland, Malignant melanoma of skin, Malignant neoplasm of uterus, Primary malignant neoplasm of cystic duct, Squamous cell carcinoma of lung, Squamous cell carcinoma of esophagus, Hepatocellular carcinoma, Malignant tumor of pancreas, Gastrointestinal stromal tumor, Malignant epithelial tumor of ovary, Lentigo maligna, Leiomyosarcoma of uterus, Malignant tumor of breast, Primary malignant neoplasm of distal bile duct, Follicular thyroid carcinoma, Malignant neoplasm of intrahepatic gall duct, Infiltrating duct carcinoma of breast, Superficial spreading malignant melanoma of skin, Malignant tumor of cervix, Inflammatory carcinoma of breast, Large cell carcinoma of lung, Cholangiocarcinoma, Primary malignant neoplasm of the peritoneum, Superficial spreading melanoma, Carcinoma of esophagus, Klatskin's tumor, Sarcoma, Siewert type III adenocarcinoma of esophagogastric junction, Malignant tumor of gallbladder, Primary malignant neoplasm of perihilar bile duct, Siewert type I adenocarcinoma of esophagogastric junction, Primary malignant clear cell tumor of ovary, Carcinosarcoma of ovary, Malignant tumor of stomach, Squamous cell carcinoma of cervix, Endometrioid carcinoma, Nodular melanoma, Adenosquamous carcinoma of cervix, Endometrioid carcinoma ovary, Adenocarcinoma of stomach, Mucinous carcinoma of breast, or Papillary thyroid carcinoma</i></p>

STUDY	DISEASE	PARTICIPANT	REPORT DATE	REPORT STATUS
haib20SL6185	Uncertain diagnosis	6185-SL-0046		Final

VARIANT

CLINICAL IMPACT

**Diagnostic of**

- Infantile fibrosarcoma

INTERPRETATION

(1) The FDA recently approved larotrectinib and entrectinib for treatment of patients with NTRK gene fusion-positive tumors, and the panel also recommends NTRK therapy options such as larotrectinib and entrectinib for patients with recurrent NTRK gene fusion-positive salivary gland tumors and distant metastases. (2) NTRK status should be evaluated in mammary analogue secretory carcinoma of the salivary gland. (3) Useful in certain circumstances as systemic therapy for NTRK gene fusion-positive recurrent disease with (a) distant metastases in patients with a performance status (PS) of 0-3, (b) unresectable locoregional recurrence or second primary with prior radiation therapy.

**NACC2, NTRK2**

NACC2-NTRK2  
fusion transcript

C

**May benefit from**

- Bevacizumab-bvzr, Bevacizumab-awwb, Bevacizumab, or Atezolizumab *in Nonsquamous non-small cell neoplasm of lung, Adenocarcinoma of lung, or Large cell carcinoma of lung*
- Pembrolizumab or Ipilimumab + Nivolumab *in Squamous cell carcinoma of lung, Adenocarcinoma of lung, Non-small cell lung cancer, Large cell carcinoma of lung, or Non-small cell carcinoma*
- Larotrectinib *in Malignant tumor of colon, Malignant tumor of lung, Invasive micropapillary carcinoma of breast, Carcinoma of salivary gland type, Endometrial carcinoma, Desmoplastic malignant melanoma, Anaplastic thyroid carcinoma, Siewert type II adenocarcinoma of esophagogastric junction, Adenocarcinoma of cervix, Nodular malignant melanoma of skin, Adenocarcinoma of pancreas, Sarcoma of soft tissue, Adenocarcinoma of lung, Primary adenocarcinoma of colon, Malignant tumor of fallopian tube, Squamous cell carcinoma of vulva, Adenocarcinoma of rectum, Infiltrating lobular carcinoma of breast, Malignant tumor of ovary, Malignant tumor of rectum, Malignant tumor of thyroid gland, Infantile fibrosarcoma, Mixed ductal and lobular carcinoma of breast, High grade endometrial stromal sarcoma, Adenocarcinoma of small intestine, Non-small cell carcinoma, Hurthle cell carcinoma of thyroid, Malignant tumor of esophagus, Non-small cell lung cancer, Malignant tumor of appendix, Acral lentiginous malignant melanoma of skin, Adenocarcinoma of esophagus, Undifferentiated sarcoma, Infiltrating carcinoma with ductal and lobular features, Malignant tumor of salivary gland, Malignant melanoma of skin, Primary*

STUDY	DISEASE	PARTICIPANT	REPORT DATE	REPORT STATUS
haib20SL6185	Uncertain diagnosis	6185-SL-0046		Final

VARIANT	CLINICAL IMPACT
	<p><i>malignant neoplasm of cystic duct, Squamous cell carcinoma of lung, Squamous cell carcinoma of esophagus, Glioblastoma, Hepatocellular carcinoma, Malignant tumor of pancreas, Gastrointestinal stromal tumor, Malignant epithelial tumor of ovary, Lentigo maligna, Leiomyosarcoma of uterus, Malignant tumor of breast, Primary malignant neoplasm of distal bile duct, Infiltrating duct carcinoma of breast, Follicular thyroid carcinoma, Malignant neoplasm of intrahepatic gall duct, Superficial spreading malignant melanoma of skin, Malignant melanoma, Malignant tumor of cervix, Inflammatory carcinoma of breast, Large cell carcinoma of lung, Cholangiocarcinoma, Primary malignant neoplasm of the peritoneum, Astrocytoma of brain, Superficial spreading melanoma, Carcinoma of esophagus, Klatskin's tumor, Siewert type III adenocarcinoma of esophagogastric junction, Malignant tumor of gallbladder, Primary malignant neoplasm of perihilar bile duct, Cholangiocarcinoma of biliary tract, Siewert type I adenocarcinoma of esophagogastric junction, Primary malignant clear cell tumor of ovary, Carcinosarcoma of ovary, Malignant tumor of stomach, Glioma, Squamous cell carcinoma of cervix, Endometrioid carcinoma, Nodular melanoma, Adenosquamous carcinoma of cervix, Endometrioid carcinoma ovary, Mucinous carcinoma of breast, Adenocarcinoma of stomach, or Papillary thyroid carcinoma</i></p> <p>— <i>Entrectinib in Malignant tumor of colon, Invasive micropapillary carcinoma of breast, Carcinoma of salivary gland type, Desmoplastic malignant melanoma, Endometrial carcinoma, Anaplastic thyroid carcinoma, Siewert type II adenocarcinoma of esophagogastric junction, Adenocarcinoma of cervix, Nodular malignant melanoma of skin, Adenocarcinoma of pancreas, Sarcoma of soft tissue, Adenocarcinoma of lung, Malignant tumor of vulva, Primary adenocarcinoma of colon, Malignant tumor of fallopian tube, Squamous cell carcinoma of vulva, Adenocarcinoma of rectum, Infiltrating lobular carcinoma of breast, Malignant tumor of ovary, Malignant tumor of rectum, Malignant neoplasm of endometrium of corpus uteri, Malignant tumor of thyroid gland, High grade endometrial stromal sarcoma, Mixed ductal and lobular carcinoma of breast, Non-small cell carcinoma, Hurthle cell carcinoma of thyroid, Neuroendocrine carcinoma, Malignant tumor of esophagus, Non-small cell lung cancer, Acral lentiginous malignant melanoma of skin, Adenocarcinoma of esophagus, Undifferentiated sarcoma, Malignant tumor of vagina, Infiltrating carcinoma with ductal and lobular features, Malignant tumor of salivary gland, Malignant neoplasm of uterus, Malignant melanoma of skin, Primary malignant neoplasm of cystic duct, Squamous cell carcinoma of lung, Squamous cell carcinoma of esophagus, Hepatocellular carcinoma, Malignant tumor of pancreas, Gastrointestinal stromal tumor, Malignant epithelial tumor of ovary, Lentigo maligna, Leiomyosarcoma of uterus, Malignant tumor of breast, Primary malignant neoplasm of distal bile duct, Follicular thyroid carcinoma, Malignant neoplasm of intrahepatic gall duct, Infiltrating duct carcinoma of breast, Superficial spreading malignant melanoma of skin,</i></p>

STUDY	DISEASE	PARTICIPANT	REPORT DATE	REPORT STATUS
haib20SL6185	Uncertain diagnosis	6185-SL-0046		Final

VARIANT

CLINICAL IMPACT

*Malignant tumor of cervix, Inflammatory carcinoma of breast, Large cell carcinoma of lung, Cholangiocarcinoma, Primary malignant neoplasm of the peritoneum, Superficial spreading melanoma, Carcinoma of esophagus, Klatskin's tumor, Sarcoma, Siewert type III adenocarcinoma of esophagogastric junction, Malignant tumor of gallbladder, Primary malignant neoplasm of perihilar bile duct, Siewert type I adenocarcinoma of esophagogastric junction, Primary malignant clear cell tumor of ovary, Carcinosarcoma of ovary, Malignant tumor of stomach, Squamous cell carcinoma of cervix, Endometrioid carcinoma, Nodular melanoma, Adenosquamous carcinoma of cervix, Endometrioid carcinoma ovary, Adenocarcinoma of stomach, Mucinous carcinoma of breast, or Papillary thyroid carcinoma*

INTERPRETATION

(1) The FDA recently approved larotrectinib and entrectinib for treatment of patients with NTRK gene fusion-positive tumors, and the panel also recommends NTRK therapy options such as larotrectinib and entrectinib for patients with recurrent NTRK gene fusion-positive salivary gland tumors and distant metastases. (2) NTRK status should be evaluated in mammary analogue secretory carcinoma of the salivary gland. (3) Useful in certain circumstances as single-agent systemic therapy for NTRK gene fusion-positive recurrent disease with (a) distant metastases in patients with a performance status (PS) of 0-3, (b) unresectable locoregional recurrence or second primary with prior radiation therapy.

POTENTIAL CLINICAL TRIALS

No relevant clinical trials were reported.

CLASSIFICATION AND LEVELS OF EVIDENCE

The variant classification system used in this report is based on joint consensus recommendations of the Association for Molecular Pathology, American Society of Clinical Oncology, and the College of American Pathologists (J Mol Diagn 2017, 19:4-23). Tiers IA, IB, IIC, IID, III and IV describe variant categories of descending clinical significance in the patient. Variants in Tier IV are not reported in accordance with the consensus recommendations.



STUDY haib20SL6185	DISEASE Uncertain diagnosis	PARTICIPANT 6185-SL-0046	REPORT DATE	REPORT STATUS Final
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IA	IB	IIC	IID
Variant of strong clinical significance, Level A evidence (FDA approved therapy or practice guideline in patient's tumor type)	Variant of strong clinical significance, Level B Evidence (consensus in the field based on well-powered studies in patient's tumor type)	Variant of potential clinical significance, Level C evidence (FDA approved therapy or practice guideline in other tumor type(s), evidence from multiple small published studies, or based on availability of investigational therapies)	Variant of potential clinical significance, Level D evidence (case reports or preclinical studies)
<b>III</b> Variant of uncertain clinical significance		<b>IV</b> Benign or likely benign variant	

## TEST DETAILS

### REPORTED GENES

A total of 523 genes were subjected to targeted next generation sequencing analysis. Details available upon request.

### CGW VERSION

CGW\_v6.13.1

### DATABASE DETAILS

The versions, releases, builds, dates of the following databases were used to generate this report.

- Genomic Build: GRCh37.p13
- Genomic Annotation Sources: NCBI RefSeq v105
- dbSNP: 149
- ExAC: v1.0
- dbNSFP: 3.5c
- NHLBI ESP: v.0.0.30
- ClinVar: 20190603
- gnomAD: r2.1
- COSMIC: v91

STUDY	DISEASE	PARTICIPANT	REPORT DATE	REPORT STATUS
haib20SL6185	Uncertain diagnosis	6185-SL-0046		Final

## METHODOLOGY

**Assay Methods:** The test was performed using the Illumina TruSight™ Oncology 500 (TSO500) targeted hybrid-capture based next generation sequencing assay. It employs Unique molecular identifiers (UMI) to enable detection of variants, present in solid tumor, formalin-fixed paraffin-embedded (FFPE) tumor, and cfDNA samples, at low VAFs with a high degree of sensitivity and specificity. TSO500 is designed to detect multiple classes of mutations including single-nucleotide variants (SNVs), multi-nucleotide variants (<3bp), small Insertions (1-18bp)/Deletions (1-27bp) and Copy Number Variants (CNVs). The assay also detects, quantitatively, microsatellite instability (MSI) and tumor mutational burden (TMB). Fusions are detected in RNA (TSO500 Solid Tumor reports only). DNA and RNA (TSO500 Solid Tumor reports) or cfDNA (cfDNA reports) extractions are performed and RNA is then reverse transcribed to cDNA. The genomic DNA and cDNA (TSO500 Solid Tumor reports) or cfDNA (TSO500 cfDNA reports) are sheared to prepare sequencing libraries. The regions of interest are hybridized to biotinylated probes, magnetically pulled down with streptavidin-coated beads, and eluted to enrich the library pool. Finally, libraries are normalized, then pooled and sequenced on an Illumina NextSeq or NovaSeq instrument.

**Secondary Analysis Methods:** The DNA and RNA data is analyzed using the Illumina Software TSO500 v2.1 Local App or the cfDNA data is analyzed using the Illumina Software TSO500 v3 Dragen Server pipeline at Discovery Life Sciences. Further processing of data for interpretation and annotation using a customized analysis pipeline within the Clinical Genomics Workspace software platform from PierianDx is then performed.

**Variant Calling:** Variants are reported according to HGVS nomenclature ([www.hgvs.org/mutnomen](http://www.hgvs.org/mutnomen)) and classified as per the AMP classification system into tiers IA, IB, IIC, IID, III and IV. These tiers are stratified by clinical utility ('actionability' for clinical decision-making as to diagnosis, prognosis, treatment options, and carrier status) and previously reported data in the medical literature. Variations found in gnomAD (<https://gnomad.broadinstitute.org/>) that have  $\geq 1\%$  minor allele frequency (except those that are also in ClinVar denoted as clinically relevant, used in a clinical diagnostic assay, or reported as a mutation in a publication) are classified as known polymorphisms. Small variant calls in the HLA-A, KMT2B, KMT2C, and KMT2D genes are filtered out due to potential mis-mapping as a result of sequence homology with other genomic regions.

### Notes:

- This assay does not detect complex structural alterations or large indels, with the exception of a subset of clinically relevant complex EGFR exon 19 indels that are specifically targeted. Variants located outside of targeted capture regions will not be detected.
- It is possible that pathogenic variants may not be reported by one or more of the tools because of the parameters used. However, tool parameters were optimized to maximize specificity and sensitivity.

## DISCLAIMER

The results provided in this report are for Research Use Only (RUO) and informational in nature. The information contained in this report cannot be used for patient treatment and/or prognostic decisions. All interpretations are made by the PierianDx Clinical Knowledgebase. No interpretations of variants have been made by Discovery Life Sciences.

The RUO assay was performed using tumor tissue; it is therefore not possible to determine whether variants detected are somatic or germline in origin unless a matched germline normal sample was analyzed using the same RUO assay

STUDY	DISEASE	PARTICIPANT	REPORT DATE	REPORT STATUS
haib20SL6185	Uncertain diagnosis	6185-SL-0046		Final

and a tumor/normal pair VCF was generated prior to PierianDx interpretation or, in cases where tumor-only sample was analyzed, a tumor-only informed bioinformatics pipeline was used to generate the VCF prior to PierianDx interpretation.

High confidence Variant Allele Fraction (VAF) cutoffs for the results provided in this report were set at 5% based on RUO verification studies performed at Discovery Life Sciences.

### PATIENT AND ORDER DETAILS

PATIENT	SPECIMEN	CASE
SEX	SPECIMEN TYPE	REVIEW STATUS
ETHNICITY	<b>Nucleic acid specimen</b>	<b>Final</b>
RACE	EXT. SPECIMEN ID	DATE ACCESSIONED
	% TUMOR IN SELECTED AREA	<b>12/04/2020 16:44</b>
		DATE REPORTED
		ACCESSION NUMBER
		<b>6185-SL-0046_rerun</b>