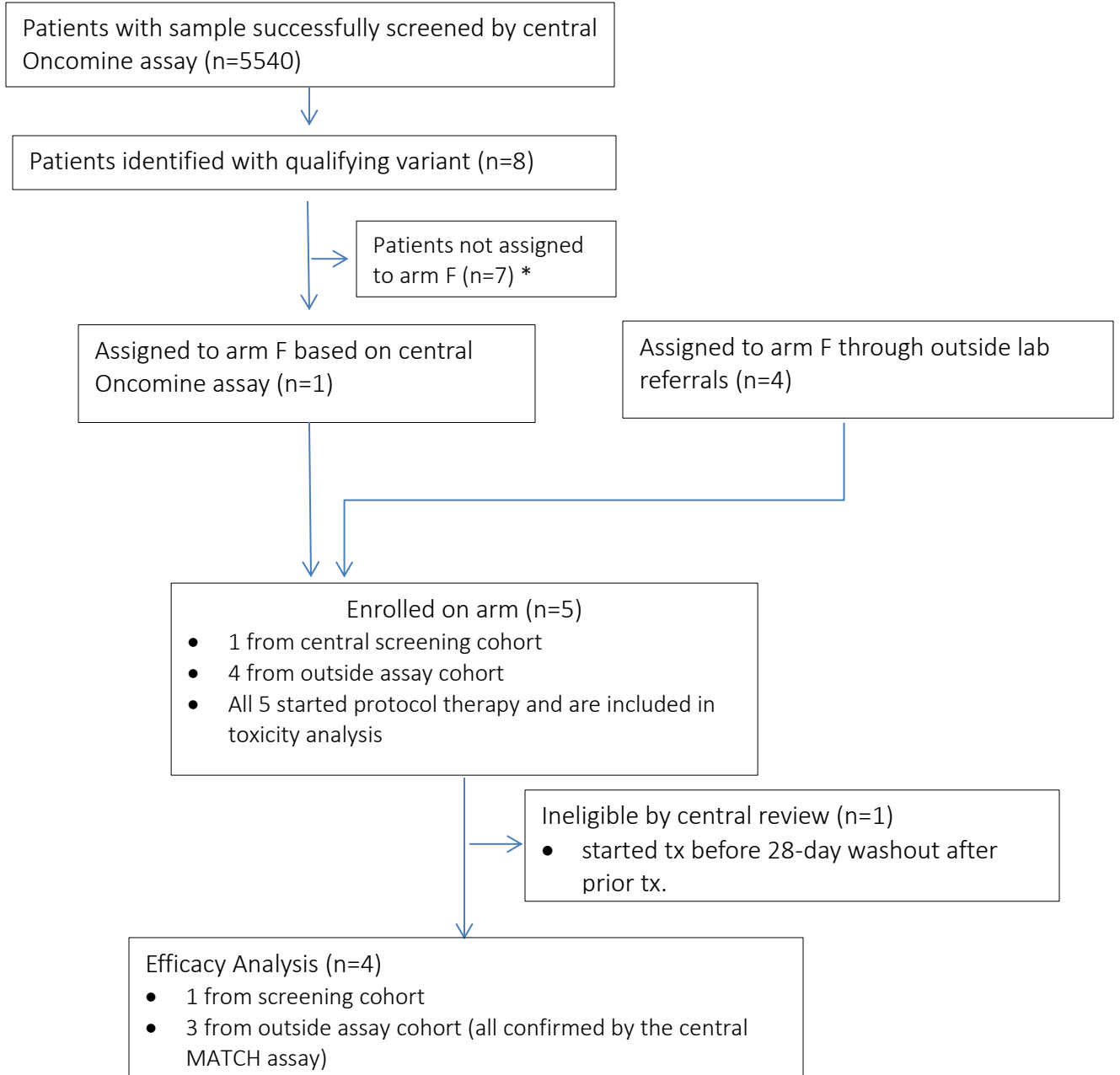
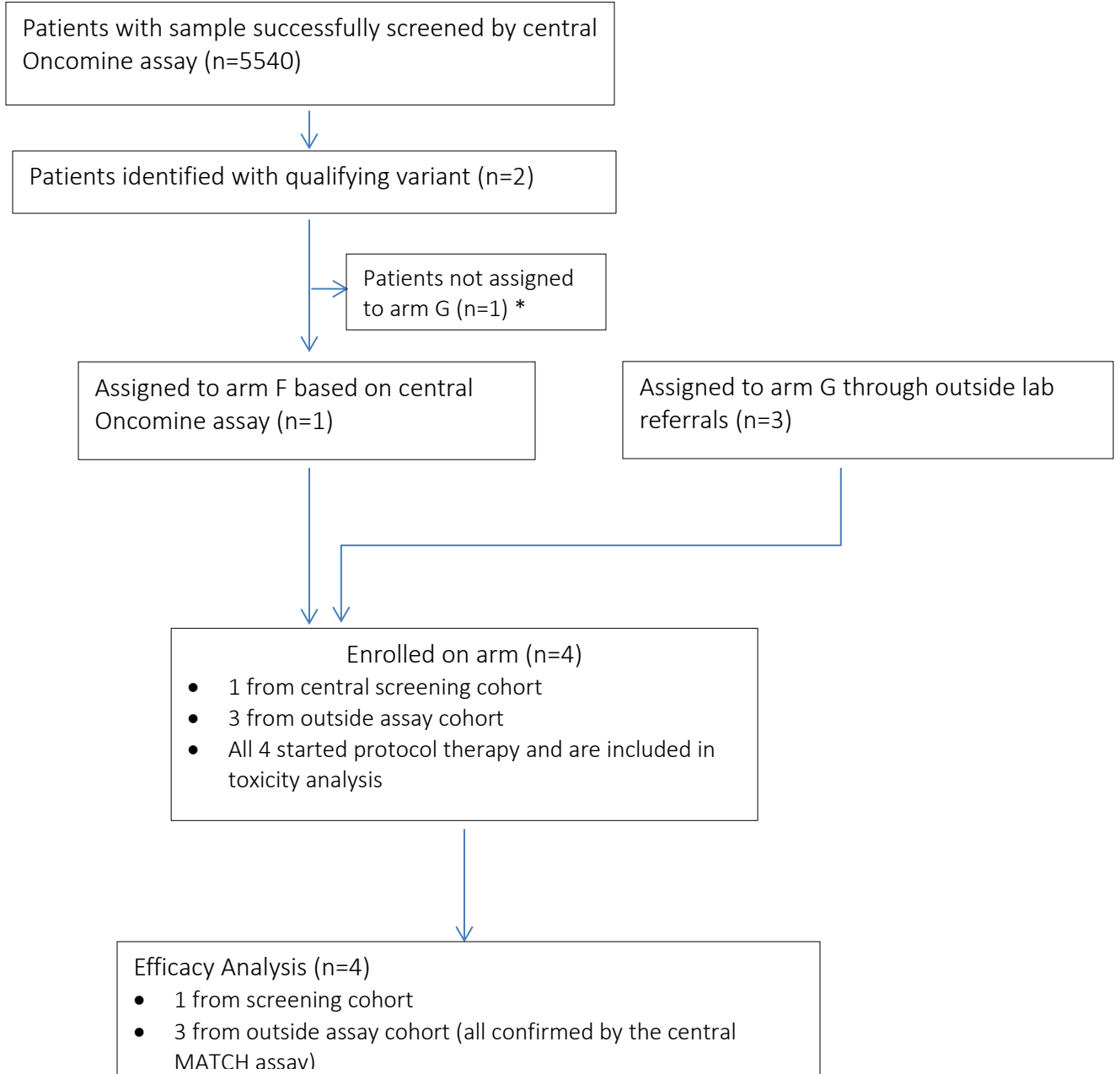


Supplemental Figure 1: Sub-protocol F (ALK) CONSORT diagram



*Reasons not receiving an assignment (all due to ineligible histology): Lung adenocarcinoma (n=7)

Supplemental Figure 2: Sub-protocol G (ROS1) CONSORT diagram



*Reasons not receiving an assignment: Not meeting the requirements of Section 3.1 of the Match Master Protocol: Patients must have ECOG performance status ≤ 1 (n=1)

Supplemental Table 1: Actionable Mutations for Sub-Protocol EAY131-F

| Gene | Variant ID |
|------|----------------------------|
| ALK | ACTG2-ALK.A2A18 |
| ALK | C2orf44-ALK.C4A20.COSF1264 |
| ALK | CLIP4-ALK.C11A23 |
| ALK | EML4-ALK.E13A20.AB462411 |
| ALK | EML4-ALK.E13A20.COSF1062 |
| ALK | EML4-ALK.E13A20.COSF408 |
| ALK | EML4-ALK.E14A20.COSF1064 |
| ALK | EML4-ALK.E14A20.COSF477 |
| ALK | EML4-ALK.E15A20.COSF413 |
| ALK | EML4-ALK.E17A20.COSF1366 |
| ALK | EML4-ALK.E17A20.COSF1367 |
| ALK | EML4-ALK.E18A20.COSF487 |
| ALK | EML4-ALK.E18A20.COSF487.1 |
| ALK | EML4-ALK.E20A20.COSF409 |
| ALK | EML4-ALK.E20A20.COSF730 |
| ALK | EML4-ALK.E2A20.COSF478 |
| ALK | EML4-ALK.E2A20.COSF479 |
| ALK | EML4-ALK.E6A17 |
| ALK | EML4-ALK.E6A18 |
| ALK | EML4-ALK.E6A19.COSF1296 |
| ALK | EML4-ALK.E6aA20.AB374361 |
| ALK | EML4-ALK.E6aA20.COSF411 |
| ALK | EML4-ALK.E6bA20.AB374362 |
| ALK | EML4-ALK.E6bA20.COSF412 |
| ALK | EML4-ALK.E7A20.NGS |
| ALK | GTF2IRD-ALK.G7A20 |
| ALK | HIP1-ALK.H21A20 |
| ALK | HIP1-ALK.H28A20 |
| ALK | KIF5B-ALK.K15A20.COSF1060 |
| ALK | KIF5B-ALK.K15A20.COSF1381 |
| ALK | KIF5B-ALK.K17A20.COSF1257 |
| ALK | KIF5B-ALK.K24A20.COSF1058 |
| ALK | KLC1-ALK.K9A20.COSF1276 |
| ALK | MEMO1-ALK.M2A7 |
| ALK | NCOA1-ALK.N21A1.NGS |
| ALK | PRKAR1A-ALK.P2A20.NGS |
| ALK | PTPN3-ALK.P2A10 |
| ALK | STRN-ALK.S3A20.COSF1430 |
| ALK | TFG-ALK.T4A20.COSF424 |
| ALK | TFG-ALK.T5A20.COSF426 |

| | |
|-----|-------------------------|
| ALK | TFG-ALK.T6A20.COSF428 |
| ALK | TPM1-ALK.T8A20.NGS |
| ALK | TPM3-ALK.T7A20 |
| ALK | TPM4-ALK.T6A20 |
| ALK | TPR-ALK.T15A20 |
| ALK | VCL-ALK.V16A20.COSF1057 |

Supplemental Table 2: Actionable Mutations for Sub-Protocol EAY131-G

| Gene | Variant ID |
|-------------|------------------------------|
| ROS1 | CCDC6-ROS1.C5R35 |
| ROS1 | CD74-ROS1.C4R33.NGS |
| ROS1 | CD74-ROS1.C6R32.COSF1202 |
| ROS1 | CD74-ROS1.C6R34.COSF1200 |
| ROS1 | CD74-ROS1.C6R35 |
| ROS1 | CEP85L-ROS1.C8R36 |
| ROS1 | CLIP1-ROS1.C19R36 |
| ROS1 | CLTC-ROS1.C31R35 |
| ROS1 | ERC1-ROS1.E11R36 |
| ROS1 | EZR-ROS1.E10R34.COSF1267 |
| ROS1 | EZR-ROS1.E10R35 |
| ROS1 | GOPC-ROS1.G4R36.COSF1188 |
| ROS1 | GOPC-ROS1.G8R35.COSF1139 |
| ROS1 | HLA_A-ROS1.H7R34 |
| ROS1 | KDEL2-ROS1.K5R35 |
| ROS1 | KDEL2-ROS1.K5Rintron34 |
| ROS1 | KIAA1598-ROS1.K11R36 |
| ROS1 | LRIG3-ROS1.L16R35.COSF1269 |
| ROS1 | MSN-ROS1.M9R34 |
| ROS1 | MYO5A-ROS1.M23R35 |
| ROS1 | PPFIBP1-ROS1.P9R35 |
| ROS1 | PWWP2A-ROS1.P1R36 |
| ROS1 | SDC4-ROS1.S2R32.COSF1265 |
| ROS1 | SDC4-ROS1.S2R34 |
| ROS1 | SDC4-ROS1.S4R32.COSF1278 |
| ROS1 | SDC4-ROS1.S4R34.COSF1280 |
| ROS1 | SLC34A2-ROS1.S13R32.COSF1259 |
| ROS1 | SLC34A2-ROS1.S13R34.COSF1261 |
| ROS1 | SLC34A2-ROS1.S13R36 |
| ROS1 | SLC34A2-ROS1.S4R32.COSF1197 |
| ROS1 | SLC34A2-ROS1.S4R34.COSF1198 |

| | |
|------|--------------------------|
| ROS1 | TFG-ROS1.T4R35 |
| ROS1 | TPM3-ROS1.T3R36 |
| ROS1 | TPM3-ROS1.T7R35.COSF1273 |
| ROS1 | ZCCHC8-ROS1.Z2R36 |

Supplemental Table 3: Response status and concurrent alterations

| Arm | Histology | Best response | Best % change | Rearrangement | # cycles | PFS event | PFS Time (mos) | Concurrent Alterations |
|-----|--|---------------|---------------|---|----------|-----------|----------------|--|
| F | Carcinoma of unknown primary site | SD | +2.4% | EML4-ALK.E6aA20.AB3 74361 & EML4-ALK.E6bA20.AB3 74362 | 1 | 1 | 2.3 | N/A |
| F | Mucinous adenocarcinoma of transverse colon | PR | -61.5% | EML4-ALK.E21A20 | 6 | 1 | 5.3 | SMAD4 p.Arg361His SMAD4 p.Arg135Ter APC p.Glu1544Ter |
| F | Leiomyosarcoma of abdominal wall arising in mitotically active leiomyoma, Müllerian type | CR | -100% | ACTG2-ALK.A2A18 | 12 | 0 | 10.8 | N/A |

| | | | | | | | | |
|---|---|----|--------|--------------------------|---|---|-----|---|
| F | Adeno-carcinoma of the rectum | PD | -3.1% | STRN-ALK.S3A20.COSF1430 | 2 | 1 | 1.7 | APC p.Arg876Ter TP53 p.Arg282Trp BRAF-BRAF fusion |
| G | Intrahepatic cholangiocarcinoma | PD | N/A* | GOPC-ROS1.G8R35.COSF1139 | 1 | 1 | 0.5 | SMAD4 p.Glu330Lys |
| G | Adeno-carcinoma of head of pancreas | PD | +5.1% | GOPC-ROS1.G8R35.COSF1139 | 2 | 1 | 1.6 | BRCA2 p.Thr3033fs*11 BRCA2 pAla938fs*21 FBXW7 p.splice site 584+2T>G |
| G | Low-grade serous adeno-carcinoma of ovary with mucin production | PR | -54.2% | GOPC-ROS1.G4R36.COSF1188 | 6 | 0 | 5.5 | NA |
| G | Adeno-carcinoma of ascending colon | SD | -13% | GOPC-ROS1.G8R35.COSF1139 | 8 | 1 | 6.9 | APC p.Leu548fsTer11 APC p.Gln1406Ter SMAD4 p.Tyr117fsTer1 SMAD4 p.Tyr117Ter TP53 p.Ser94Ter |

Supplemental Table 4: Toxicities at least possibly related to treatment

| Toxicity Type | Treatment Arm | | | | | | | | | | | |
|---|----------------|----------|----------|----------|----------------|----------|----------|----------|-------------|----------|----------|----------|
| | EAY131-F (n=5) | | | | EAY131-G (n=4) | | | | Total (n=9) | | | |
| | Grade | | | | Grade | | | | Grade | | | |
| | 1,2 (n) | 3 (n) | 4 (n) | 5 (n) | 1,2 (n) | 3 (n) | 4 (n) | 5 (n) | 1,2 (n) | 3 (n) | 4 (n) | 5 (n) |
| Anemia | 1 | - | - | - | 1 | - | - | - | 2 | - | - | - |
| Sinus bradycardia | 2 | - | - | - | - | - | - | - | 2 | - | - | - |
| Dry eye | - | - | - | - | 1 | - | - | - | 1 | - | - | - |
| Eye disorders - Other, specify | 1 | - | - | - | - | - | - | - | 1 | - | - | - |
| Flashing lights | 1 | - | - | - | - | - | - | - | 1 | - | - | - |
| Photophobia | 1 | - | - | - | - | - | - | - | 1 | - | - | - |
| Abdominal distension | 1 | - | - | - | - | - | - | - | 1 | - | - | - |
| Abdominal pain | 1 | - | - | - | - | 1 | - | - | 1 | 1 | - | - |
| Bloating | - | - | - | - | 1 | - | - | - | 1 | - | - | - |
| Constipation | 1 | - | - | - | 1 | - | - | - | 2 | - | - | - |
| Diarrhea | 3 | - | - | - | 1 | - | - | - | 4 | - | - | - |
| Dyspepsia | - | - | - | - | 1 | - | - | - | 1 | - | - | - |
| Gastrointestinal disorders - Other, specify | 1 | - | - | - | - | - | - | - | 1 | - | - | - |
| Hemorrhoids | - | - | - | - | 1 | - | - | - | 1 | - | - | - |
| Nausea | 3 | - | - | - | 1 | - | - | - | 4 | - | - | - |
| Vomiting | 1 | - | - | - | 1 | - | - | - | 2 | - | - | - |
| Fatigue | 2 | - | - | - | 2 | - | - | - | 4 | - | - | - |
| Fever | - | - | - | - | 1 | - | - | - | 1 | - | - | - |
| General disorders and administration site conditions - Other, specify | 1 | - | - | - | - | - | - | - | 1 | - | - | - |
| Edema limbs | 1 | - | - | - | 1 | - | - | - | 2 | - | - | - |
| Alanine aminotransferase increased | 3 | - | 1 | - | 1 | - | - | - | 4 | - | 1 | - |
| Alkaline phosphatase increased | 3 | - | - | - | 1 | - | - | - | 4 | - | - | - |
| Aspartate aminotransferase increased | 2 | 1 | 1 | - | 1 | - | - | - | 3 | 1 | 1 | - |
| Blood bilirubin increased | 1 | - | 1 | - | - | - | - | - | 1 | - | 1 | - |

| Toxicity Type | Treatment Arm | | | | | | | | | | | |
|---------------------------------|----------------|----------|----------|----------|----------------|----------|----------|----------|-------------|----------|----------|----------|
| | EAY131-F (n=5) | | | | EAY131-G (n=4) | | | | Total (n=9) | | | |
| | Grade | | | | Grade | | | | Grade | | | |
| | 1,2 (n) | 3 (n) | 4 (n) | 5 (n) | 1,2 (n) | 3 (n) | 4 (n) | 5 (n) | 1,2 (n) | 3 (n) | 4 (n) | 5 (n) |
| Creatinine increased | - | - | - | - | 1 | - | - | - | 1 | - | - | - |
| Investigations - Other, specify | 1 | - | - | - | - | - | - | - | 1 | - | - | - |
| Lymphocyte count decreased | 2 | - | - | - | - | 1 | - | - | 2 | 1 | - | - |
| Platelet count decreased | - | - | - | - | 1 | - | - | - | 1 | - | - | - |
| Weight gain | - | - | - | - | 1 | - | - | - | 1 | - | - | - |
| Weight loss | - | - | - | - | 1 | - | - | - | 1 | - | - | - |
| White blood cell decreased | 1 | - | - | - | 2 | - | - | - | 3 | - | - | - |
| Anorexia | 1 | - | - | - | 1 | - | - | - | 2 | - | - | - |
| Hyperglycemia | 1 | - | - | - | - | - | - | - | 1 | - | - | - |
| Hyperkalemia | - | - | - | - | 1 | - | - | - | 1 | - | - | - |
| Hypoalbuminemia | 2 | - | - | - | 2 | - | - | - | 4 | - | - | - |
| Hypocalcemia | 2 | - | - | - | 1 | - | - | - | 3 | - | - | - |
| Hypoglycemia | 1 | - | - | - | - | - | - | - | 1 | - | - | - |
| Hypokalemia | - | - | - | - | 1 | - | - | - | 1 | - | - | - |
| Hypomagnesemia | - | - | - | - | 2 | - | - | - | 2 | - | - | - |
| Hyponatremia | - | - | 1 | - | 1 | - | - | - | 1 | - | 1 | - |
| Hypophosphatemia | - | 1 | - | - | - | - | - | - | - | 1 | - | - |
| Dysgeusia | 1 | - | - | - | - | - | - | - | 1 | - | - | - |
| Headache | 1 | - | - | - | 1 | - | - | - | 2 | - | - | - |
| Acute kidney injury | - | - | - | - | - | 1 | - | - | - | 1 | - | - |
| Nasal congestion | 1 | - | - | - | - | - | - | - | 1 | - | - | - |
| Rash acneiform | 1 | - | - | - | - | - | - | - | 1 | - | - | - |
| Rash maculo-papular | - | - | - | - | 1 | - | - | - | 1 | - | - | - |
| Hypertension | - | - | - | - | 1 | - | - | - | 1 | - | - | - |
| WORST DEGREE | 3 | 1 | 1 | - | 2 | 2 | - | - | 5 | 3 | 1 | - |

Supplemental Table 5:**Frequencies of ALK and ROS1 rearrangements (excluding NSCLC and lymphoma)**

| | ALK | ROS1 |
|--|----------------------|----------------------|
| Vendor 1 | 1.3x10 ⁻³ | 5.6x10 ⁻⁴ |
| Vendor 2 | 7.4x10 ⁻⁴ | 1.6x10 ⁻⁴ |
| Vendor 3 | 6.0x10 ⁻⁴ | 2.0x10 ⁻⁴ |
| Combined frequencies from two vendors | | |
| | 1.0x10 ⁻³ | 4.0x10 ⁻⁴ |

Supplemental Table 6:**Expanded cohort of ALK-rearrangements (excluding NSCLC and lymphoma)**

| Malignancy | # cases | Proportion of all ALK cases |
|---------------------------------------|----------------|------------------------------------|
| Thyroid Carcinoma | 6 | 0.162162 |
| Colorectal Adenocarcinoma | 5 | 0.135135 |
| Soft Tissue Tumor | 5 | 0.135135 |
| Pancreatic Adenocarcinoma | 4 | 0.108108 |
| Cancer of Unknown Primary | 3 | 0.081081 |
| Female Genital Tract Malignancy | 3 | 0.081081 |
| Ovarian Surface Epithelial Carcinoma | 2 | 0.054054 |
| Uterine Serous Carcinoma | 2 | 0.054054 |
| Bladder Cancer - Urothelial | 1 | 0.027027 |
| Gastrointestinal Stromal Tumor (GIST) | 1 | 0.027027 |
| Kidney Cancer | 1 | 0.027027 |
| Lung Small Cell Cancer (SCLC) | 1 | 0.027027 |
| Melanoma | 1 | 0.027027 |
| Retroperitoneal or Peritoneal Sarcoma | 1 | 0.027027 |
| Salivary Gland Tumors | 1 | 0.027027 |

Supplemental Table 7:**Expanded cohort of ROS1-rearrangements (excluding NSCLC and lymphoma)**

| Malignancy | # cases | Proportion of all ROS1 cases |
|---------------------------|----------------|-------------------------------------|
| Glioblastoma | 8 | 0.5 |
| Breast Carcinoma | 2 | 0.125 |
| Cancer of Unknown Primary | 1 | 0.0625 |
| Cholangiocarcinoma | 1 | 0.0625 |
| Colorectal Adenocarcinoma | 1 | 0.0625 |
| Pancreatic Adenocarcinoma | 1 | 0.0625 |
| Soft Tissue Tumor | 1 | 0.0625 |
| Thyroid Carcinoma | 1 | 0.0625 |

Supplemental Table 8: TMB of expanded molecular cohort

| TMB | # cases | Proportion |
|---------------|----------------|-------------------|
| Intermediate | 26 | 0.490566 |
| Low | 22 | 0.415094 |
| High | 2 | 0.037736 |
| QNS | 2 | 0.037736 |
| Indeterminate | 1 | 0.018868 |

QNS: quantity not sufficient

Supplemental Table 9: MSI of expanded molecular cohort

| MSI | # cases | Proportion |
|---------------|----------------|-------------------|
| Stable | 49 | 0.924528 |
| QNS | 2 | 0.037736 |
| High | 1 | 0.018868 |
| Indeterminate | 1 | 0.018868 |

QNS: quantity not sufficient