NRG1 Fusions in Solid Tumors

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Background

• NRG1 gene fusions are rare but actionable genomic drivers that occur across a growing number of tumor types.

• NRG1 has an EGF-like domain that serves as a ligand for ErbB (HER3) receptors, thereby inducing heterodimerization, usually with HER2, and subsequent activation of relevant downstream signaling pathways.

• Agents targeting the HER2/HER3 pathway have shown early clinical promise in NRG1 fusion-positive cancers.

The HER2/HER3 bispecific antibody nectuzumab has FDA Fast Track Designation for tumors with NRG1 fusions.

Objectives and Methods

• Samples were submitted for clinical molecular profiling at Caris Life Sciences via Caris MI Tumor Seek (Phoenix, AZ).

• Gene fusion detection was performed on mRNA isolated from a formalin-fixed paraffin-embedded tumor sample using the illumina NovaSeq platform (Illumina, Inc., San Diego, CA) and Agilent SureSelect Human All Exon V7 bait panel (Agilent Technologies, Santa Clara, CA).

• All NRG1 fusions with ≥ 3 junction reads were identified for manual review and for characterization of fusion class, intact functional domains, domain prediction, breakpoints, frame retention and co-occurring alterations by next-generation sequencing.

Conclusions

• Among the 261 unique tumors with an NRG1 fusion, there were 153 unique fusion partners.

• There are a wide variety of fusion partners within and across tumor types.

• The clinical implications of the heterogeneity among fusion partners warrants further investigation.

Abstract #3132

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Results

Among the 261 unique tumors with an NRG1 fusion, there were 153 unique fusion partners.

Figure 3. NRG1 fusion prevalence by tumor type

Figure 1. Detected NRG1 fusion positive tumors by type

Figure 2. NRG1 fusion partners

Table 1. NRG1 fusion partners

Table 2. NRG1 fusion prevalence by tumor type

Table 3. Co-altered genes

Reference