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# 1191O MRTX-500: Phase II trial of sitravatinib (sitra) + nivolumab (nivo) in patients (pts) with non-squamous (NSQ) non-small cell lung cancer (NSCLC) progressing on or after prior checkpoint inhibitor (CPI) therapy

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# NSCLC, METASTATIC

## 1191O MRTX-500: Phase II trial of sitravatinib (sitra) + nivolumab (nivo) in patients (pts) with non-squamous (NSQ) non-small cell lung cancer (NSCLC) progressing on or after prior checkpoint inhibitor (CPI) therapy

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**Background:** Therapy with CPI has improved OS across many tumor types, including in a subset of pts with NSCLC. Mechanisms of CPI resistance, however, have been described, including an immunosuppressive TME, which may include recruitment of immunosuppressive myeloid-derived suppressor cells (MDSCs), regulatory T cells (Tregs), and M2-polarized macrophages within the TME. Sitra, a spectrum-selective TKI targeting TAM (Tyro3/Axl/MerTK) receptors and VEGFR2, reduces the number of MDSCs and Tregs while increasing the ratio of M1/M2-polarized macrophages, and thus is hypothesized to overcome an immunosuppressive TME and augment antitumor immune responses.

**Methods:** MRTX-500 (NCT02954991) is a phase II study evaluating sitra (120 mg QD) + nivo (Q2W or Q4W) in pts with NSQ NSCLC who have progressed on or after treatment, with a CPI-based regimen (anti-PD1/PD-L1) and/or platinum doublet chemotherapy. The primary endpoint is ORR per RECIST 1.1. Secondary endpoints include OS, PFS, and safety. We report updated efficacy data for pts with NSCLC with PCB (prior clinical benefit; CR, PR, or SD $\geq$12 weeks) from a CPI who were treated with sitra + nivo as either 2L or 3L therapy.

**Results:** As of 17 October 2020, 68 pts with PCB (57% female; median age, 66 years; ECOG PS 0/1/2, 27%/66%/7%) were treated. Median follow-up was 28 months, median OS was 15 months (95% CI 9.3, 21.1),1- and 2-year OS rates were 56% and 32%, respectively. Median PFS was 6 months, and ORR was 16% (11/68), including 2 CRs. Median duration of response was 13 months. In all CPI-experienced pts evaluable for safety (n=124), treatment related adverse events (TRAEs) occurred in 91% of pts, with Gr 3/4 TRAEs occurring in 60% of pts. The most common ($\geq$10%) Gr 3/4 TRAEs were hypertension and diarrhea. There were no Gr 5 TRAEs. Discontinuation rates for sitra and nivo due to any AE were 30% and 27%, respectively.

**Conclusions:** Sitra + nivo demonstrated antitumor activity and encouraging OS compared to historical controls and no new safety signals were observed in pts with NSQ NSCLC who progressed on prior CPI. This combination is being evaluated in the phase III SAPPHIRE study.

**Clinical trial identification:** NCT02954991.

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