



Healthcare

ASTRAZENECA (NEUTRAL, FV 6480p) | Do CM-227 raise chances to see NEPTUNE and POSEIDON positive?

- Later this year, AZ is expected to report data from two significant phase III trials which are evaluating durvalumab in stage IV NSCLC. And what BMS reported a couple of days ago with CM-227 is encouraging for NEPTUNE to be equally positive since it is testing a similar IO-IO combination (durva-treme) vs SoC CT in 1L NSCLC. That said, there is a difference in the selection of patients since the part Ia of CM-227 only considered patients with PD-L1 overexpression (PD-L1>1%) whereas NEPTUNE is measuring the benefit (still in OS) in patients with high TMB. But the literature says that high TMB is a relatively good marker to predict response to IO, the point being more about the relevance of the results in clinical practice since PD-L1 testing looks more easy and popular today. Moreover the fact that NEPTUNE is not looking at each compound individually will not make discussions with regulators easy.
- From that perspective, the construction of POSEIDON is more robust and is largely inspired by the success of the IO-CT combinations, mixing all views i.e. the IO-IO hypothesis to try show some synergy but in combination with CT since MYSTIC showed that IO-IO without CT was not potent enough while having also a IO-CT arm to mimic KN-189 which is new SoC in the field. From that perspective, the failure of CM-227 part 2 comes a bit as a surprise since Opdivo-CT failed to show superiority over CT alone in non-squamous NSCLC patients, regardless of PD-L1 status.
- During the call yesterday, AZ representatives were very cautious about the interpretations to give to CM-227 ahead of the detailed results (likely to be presented at ESMO), stressing the high degree of inconsistencies across trials.

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