Evaluate Vantage

September 28, 2015

ECC – Roche puts the atezo pieces together

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The European Cancer Congress has been primarily the atezolizumab showcase this year, with Roche adding strength to its filing case by reporting data in bladder cancer where its immuno-oncology agent has differentiated itself from rivals from Merck & Co and Bristol-Myers Squibb.

This ought to raise questions about the Swiss group's regulatory strategy: whether to go first in the rather small space of bladder cancer or go after the big prize of non-small lung cancer. Greater efficacy in PD-L1-expressing patients compared with others could also mean a limited label, although it is worth noting that similarly acting agents Keytruda and Opdivo have achieved approval in metastatic melanoma without restrictions to the biomarker positives (*ECC – Roche looks ready for the PD-L1 lung cancer chase, September 27, 2015*).

The phase II IMVigor trial on Sunday reported that in the all-comers population of locally advanced or metastatic urothelial carcinoma patients, on an intent-to-treat basis, atezolizumab achieved a 15% objective response rate, the primary endpoint. In high and intermediate PD-L1 expression patients the rate was 27%, and 18% in patients with any expression of this biomarker.

Outcomes

This appeared to have no effect on disease progression, with 2.1 months of progression-free survival in each of these three groups. The data are not mature enough to make a judgement on overall survival, as the median has not been met for high and intermediate expression patients.

Little difference in overall survival could be seen between all-comers and patients with any degree of PD-L1 progression, with a median of 7.9 months for the former and eight for the latter.

Regulators and researchers view survival as the gold standard, of course, so a case could be made for Roche to file the antibody in all comers. Effectiveness of drugs acting on the PD-1/PD-L1 checkpoint in non-expressing patients, limited though it might be, has been a controversial topic in oncology circles, and for now regulators have not come down firmly on either side.

The FDA's approval of Opdivo and Keytruda in melanoma without specifying PD-L1 expression has been conditional and subject to revision following the delivery of additional data, which could include biomarker measurement. The European Medicines Agency's recent vote in support of Opdivo in second-line non-small cell lung cancer did not specify PD-L1 expression.

Roche, of course, is mum on how it plans to approach regulators, stating in similar wording in press releases about the studies in bladder and lung cancers that it would submit the data to global authorities.

In lung cancer Roche is almost certain to be third to market, as Merck's Keytruda is due an FDA decision this week and Bristol-Myers' Opdivo around the new year. In bladder cancer – forecast to be just a $169m market in 2020, according to *EvaluatePharma* – the competition is less intense, with Lilly's anti-VEGF antibody Cyramza offering the only potential resistance, and this is not likely to report pivotal data until 2017.

Having breakthrough designation in both indications will help guide Roche's next steps. The US agency's views of the robustness of the data across indications and patient groupings ought to be made clear in the coming weeks. The precedent set so far by Opdivo and Keytruda decisions suggests that the regulators will err on the side of wider acceptance.

Study	Trial ID
IMVigor	NCT02108652

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