Evaluate Vantage

December 04, 2017

# Event – Roche's Immotional bid to avoid Bristol's renal controversy

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First-line kidney cancer became a contentious area for anti-PD-(L)1 drugs after Opdivo's Checkmate-214 result was presented at Esmo. Next up is Roche's Tecentriq, the Immotion-151 study of which should shed more light on just how relevant PD-(L)1 blockade is in this setting.

Though Immotion-151 is due shortly to show whether Tecentriq has a future in kidney cancer it does not seem to be the subject of major focus by the sellside. Moreover, the trial should indicate whether the Roche drug works across subjects with different disease prognoses, and whether Avastin has an important role to play as part of a combo.

An obvious parallel exists with Roche's first-line NSCLC trial Impower-150, which read out positively two weeks ago, showing that the Tecentriq/Avastin combo was a goer. However, beyond the mechanistic concept, there might be limited readacross from lung to renal cancer.

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|---|---|
| **Product** | Tecentriq |
| **Company** | Roche |
| **Product NPV** | $3.7bn* |
| **% of market cap** | 2% |
| **Event** | Results from Immotion-151 trial in 1st-line renal cancer in combination with Avastin |
| **Date** | Late 2017/early 2018 |
| *Note: *based on $726m 2022 sales consensus in all renal cancer settings.* | |

The logic of a combo in first-line renal cancer has already been demonstrated by Opdivo plus Yervoy, though Bristol's Checkmate-214 result did not come without controversy (*Esmo 2017 – Renal cancer battlefront moves to the front line, September 11, 2017*).

Bristol's data raised two questions: does checkpoint blockade work in favourable-risk patients, and are PD-L1-negative subjects actually better off on Pfizer's Sutent? Checkmate-214 showed a strong survival benefit for Opdivo plus Yervoy in intermediate/poor-prognosis patients, but in favourable-risk subjects there seemed to be no benefit, and the dataset was driven by PD-L1-positives.

At least Roche will have partly avoided the second question. While Immotion-151 recruits all comers, the co-primary progression-free survival endpoint relates specifically to subjects expressing PD-L1 at 1% or above; the overall survival co-primary is in all comers, while OS in PD-L1 >1% subjects is a key secondary measure, all versus Sutent. However, the inclusion criteria for the trial make no specific recommendation as to disease prognosis.

The chances of success are high, judging by results from the smaller Immotion-150 trial. This showed a remission rate benefit for Tecentriq plus Avastin over Sutent, the first-line standard of care – but only in PD-L1-positive subjects; there was no benefit in all-comers, or for Tecentriq alone in any group, though the data were complicated by patient crossover.

Followers of the Roche trial will also need to keep an eye on Exelixis/Ipsen's Cabometyx, which scored a remarkable success in the first-line renal cancer Cabosun trial a year ago, and faces a US FDA verdict for front-line use on February 15. Cabosun showed a progression-free survival benefit for Cabometyx over Sutent, but only recruited intermediate/poor-prognosis patients.

**Upper hand**

Still, however controversial Bristol's Checkmate-214 study was, it cannot be denied that Opdivo has the upper hand.

Its Checkmate-025 study was the first of a checkpoint MAb to show a survival benefit in renal cell carcinoma, and on the strength of this the Bristol drug secured the US green light in the second-line setting in November 2015. No other checkpoint MAb has any renal cancer setting on its label.

Of course, Roche is not alone in trying. And in first-line renal cell carcinoma several immuno-oncology agents are being studied – all in combination trials, but only some specifically in PD-L1-expressing patients.

Since Bristol and Roche have already demonstrated the importance of the PD-L1 biomarker in this cancer, competitors recruiting all-comers will need to tread carefully. For Immotion-151 the main question will be how enrolled patients' disease prognosis might affect the result.

**Selected phase III 1st-line renal cell carcinoma studies**

| Study | Project(s) | Sponsors | Enrolment | Co-primary endpoints | Trial ID |
|---|---|---|---|---|---|
| Checkmate-214 | Opdivo + Yervoy | Bristol-Myers Squibb | 1,407, all comers | OS, PFS & ORR vs Sutent | NCT02231749 |
| Immotion-151 | Tecentriq + Avastin | Roche | 915, PD-L1 <1% | OS & PFS vs Sutent | NCT02420821 |
| Javelin Renal 101 | Avelumab + Inlyta | Pfizer/MerckKGaA | 830, PD-L1-positives | OS & PFS vs Sutent | NCT02684006 |
| Keynote-426 | Keytruda + Inlyta | Merck & Co | 840, all comers | OS & PFS vs Sutent | NCT02853331 |
| Keynote-679 | Keytruda + epacadostat | Merck & Co | 630, all comers | OS & PFS vs Sutent or Votrient | NCT03260894 |

*This story has been corrected to reflect the design of Immotion-151.*

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