Evaluate Vantage

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A possible edge for Keytruda in adjuvant lung cancer

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After Roche's US approval for Tecentriq in adjuvant NSCLC attention turned to Merck & Co's Keynote-091 trial of Keytruda in the same setting. Today Merck unveiled a positive result that could give Keytruda an edge: while Tecentriq's Impower-010 trial supported approval only in PD-L1-expressing patients with stage II-IIIA disease, Keynote-091 appears to be positive in all-comers at stages IB-IIIA. Keynote-091 has disease-free survival versus chemo as primary efficacy measure, split between co-primary endpoints in all-comers and in PD-L1 ≥50% expressers, and an interim analysis has concluded that the former is positive. DFS in PD-L1 ≥50% expressers "did not meet statistical significance per the pre-specified statistical plan", Merck said. However, this could be a quirk as the interim efficacy bar is likely high, and there might be a relatively low number of events at this point. Potentially more important questions are how Keytruda performed in stage IB patients and in PD-L1 non-expressers, given that Tecentriq had no activity in the former and showed an illusory benefit in the latter. Next up in adjuvant NSCLC are readouts from Bristol Myers Squibb's Checkmate-77T and Astrazeneca's Mermaid-1 studies.

Selected anti-PD-(L)1 MAb studies in adjuvant NSCLC

Drug	Study	Design	Primary endpoint(s)	Result
Tecentriq	Impower-010	Chemo combo vs chemo; stage IB-IIIA disease	DFS in stage II-IIIA PD-L1 ≥1% expressers, stage II-IIIA all-comers & stage IB-IIIA all-comers (sequential)	Positive in stage II-IIIA PD-L1 ≥1% expressers (US approved 15 Oct 2021)
Keytruda	Keynote-091 (Pearls)	MonoRx (chemo optional) vs chemo; stage IB-IIIA disease	DFS in all-comers & ≥50% PD-L1 expressers (co-primaries)	At interim, positive in all-comers but not in ≥50% PD-L1 expressers
Opdivo	Checkmate-77T	Neoadjuvant chemo combo, then monoRx, vs chemo; stage II-IIIB disease	DFS	2023-24 readout
Imfinzi	Mermaid-1	Chemo combo vs chemo; stage II-III disease	DFS in PD-L1 ≥1% expressers	2024 readout

Source: company filings, clinicaltrials.gov & analyst expectations of timing.