Evaluate Vantage

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Asco-GU – Clear blue water between Keytruda and kidney cancer rivals

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Merck & Co/Eisai's Clear study results look better than Bristol/Exelixis's Checkmate-9ER, but the big loser could be Pfizer.

In the seesawing battle for control of the front-line kidney cancer market Merck & Co just reinforced its lead, courtesy of full data from the Clear/Keynote-581 study, just presented at the Asco-GU meeting.

The results show a stunning 61% reduction in risk of progression or death for Keytruda combined with Eisai's tyrosine kinase inhibitor Lenvima, versus Sutent, Pfizer's aging first-line standard of care. The data suggest Merck/Eisai edging out Bristol Myers Squibb/Exelixis, but it could be that Pfizer is actually hit harder, and not because of Sutent.

The reason is that, on a cross-trial basis, it can be argued that Bristol/Exelixis's Opdivo plus Cabometyx combo still holds its own. But another first-line newcomer, Pfizer's Bavencio plus Inlyta, looks distinctly inferior; and, with the Clear study under its belt, Merck no longer has any need to promote the benefits of combining Keytruda with Pfizer's Inlyta.

Until the Clear readout the performance of Keytruda plus Inlyta in the Keynote-426 trial had been Merck's best defence against Bristol/Exelixis. The latter companies had reported highly positive data at Esmo meeting from the Checkmate-9ER study, on the basis of which their combo secured a first-line label in January (*Esmo 2020 puts Opdivo and Cabometyx back in the game, September 19, 2020*).

A four-way battle in first-line kidney cancer				
	Checkmate-9ER*	Keynote-426**	Javelin Renal 101^	Clear/Keynote-581^^
PD-(L)1 + TKI combo	Opdivo + Cabometyx	Keytruda + Inlyta	Bavencio + Inlyta	Keytruda + Lenvima
Companies	BMS/Exelixis/Ipsen	Merck & Co/Pfizer	Merck KGaA/Pfizer	Merck & Co/Eisai
Median PFS vs Sutent (mth)	16.6 vs 8.3	17.1 vs 11.1	13.3 vs 8.0	23.9 vs 9.2
Hazard ratio for PFS	0.51	0.69	0.69	0.39
Median OS vs Sutent (mth)	NR vs NR	NR vs NR	NR vs NR	NR vs NR
Hazard ratio for OS	0.60	0.59	0.80	0.66
*Sources: *Esmo 2020; **EMA report; ^Ann Oncol, Aug 2020; ^^Asco-GU 2021.*				

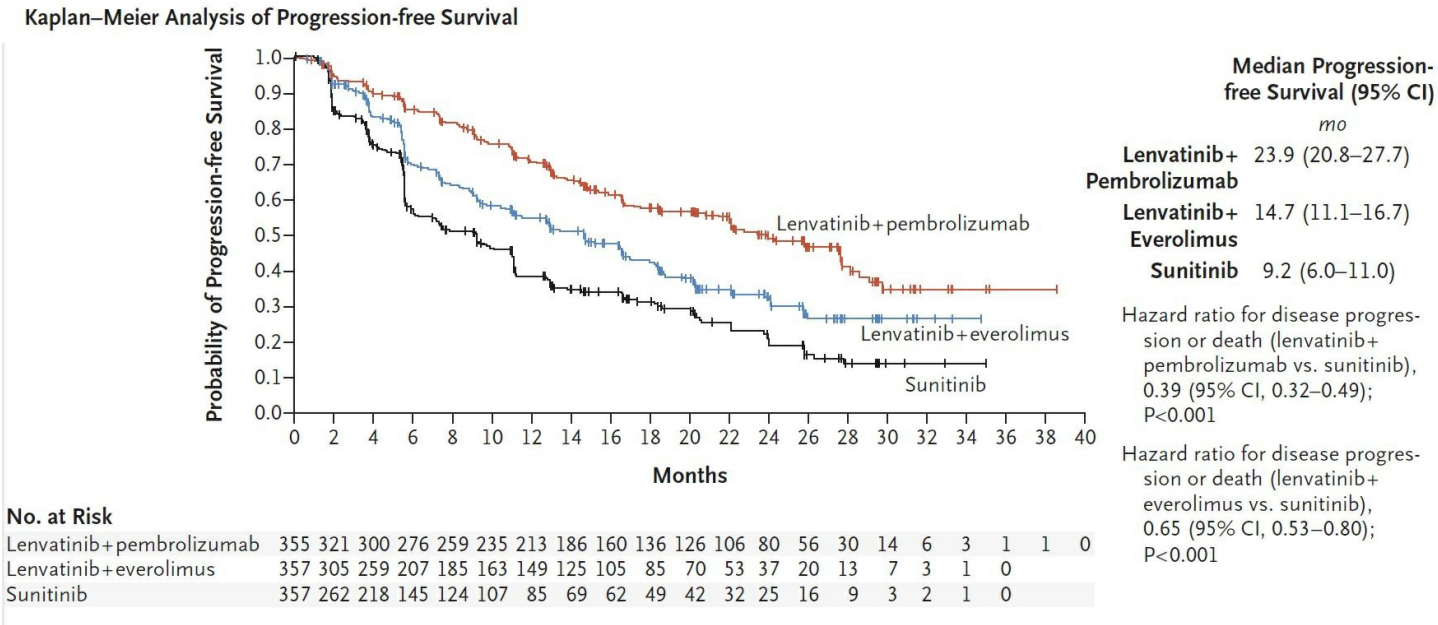
But now Merck reps can legitimately argue that Eisai's Lenvima is the TKI of choice in first-line renal cancer combinations.

Clear had been toplined positive last November, and full data a Asco-GU show the combo scoring median PFS of nearly two years, higher on a cross-trial basis than Keytruda plus Inlyta, and than Opdivo plus Cabometyx.

None of the battling four datasets are sufficiently mature to have reached median overall survival, so all that can be said for now is that the hazard ratios look broadly similar, except for that in Bavencio's Javelin Renal 101.

Eisai might now also try to make the case for Lenvima without PD-1 blockade in the front-line setting; its drug has a second-line label, but one of Clear's three cohorts tested it without Keytruda, and this showed a statistically significant mPFS benefit of 14.7 versus 9.2 months. However, the lack of an OS benefit (HR=1.15) might put paid to such plans, at least on the current data.

As is to be expected, the TKI was associated with high levels of toxicity, with serious treatment-related adverse events seen in 72-73% of patients in two Lenvima cohorts, versus 59% for Sutent. The debate around which combo is best now looks to turn to differences in the various trial subjects' baseline characteristics.



Source: Dr Robert Motzer & NEJM.

An earlier version of this story showed an incorrect hazard ratio for progression or death.

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