Evaluate Vantage

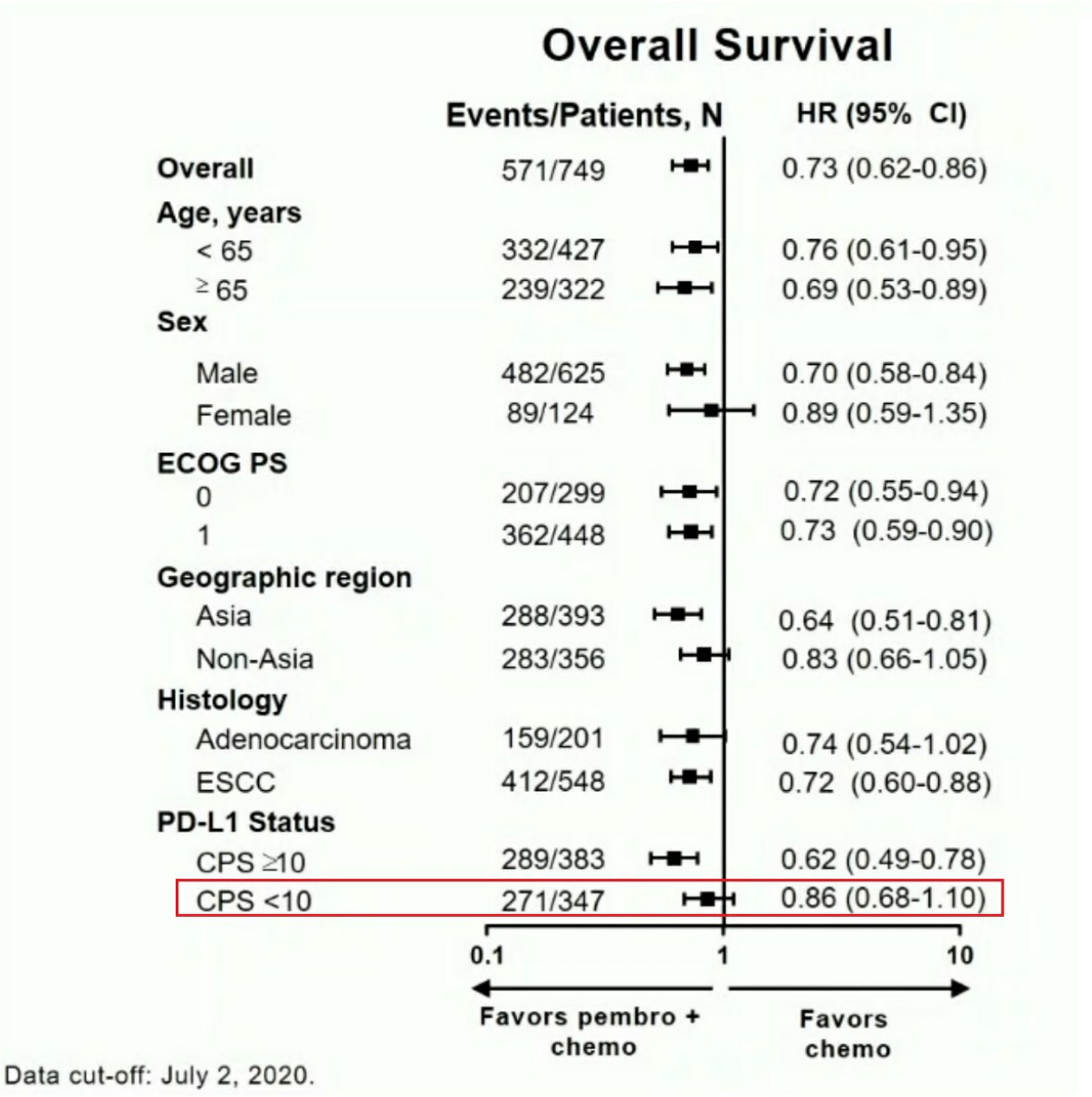
May 25, 2021

Europe’s regulator looks tougher than its US counterpart, again

Jacob Plieth

Restricting Keytruda’s front-line oesophageal cancer label to ≥10% PD-L1 expressers, as the EU is proposing to do, makes perfect sense given the available data. This would put the regulator, whose CHMP recommendation was revealed yesterday, at odds with the US FDA, which in March approved Merck & Co’s drug in this cancer in all-comers. At issue is the supporting study, Keynote-590, in first-line oesophageal/gastroesophageal junction carcinoma (*Esmo 2020 – double win complicates the gastric cancer picture, September 21, 2020*). This showed a survival benefit in ≥10% PD-L1 expressers and in all-comers. But subgroup data presented at Esmo suggested that an exceptionally strong result in PD-L1 expressers drove the all-comers result: in subjects expressing PD-L1 at below 10% the confidence interval’s upper bound for overall survival was above 1.00, meaning that some patients might have been better off on chemo alone. While it is possible that many 1-10% PD-L1 expressers did derive a benefit, the CHMP is – not for the first time – proposing a tougher line than the FDA. And for doctors the gastroesophageal cancer space is further complicated by the recent US approval of Keytruda plus Herceptin in Her2-positive patients, and by that of adjuvant Opdivo.

Survival in Key Subgroups



Source: Keynote-590 slide adapted from Dr Peter Enzinger & Esmo.