CRC Abstracts – RAS Viewpoint

Key Trial Readouts

👎	**Napa+FOLFIRI +/- bev in 2L**: napabucasin failed as a monotherapy in an early stage trial in 2016. The company had switched gears and immediately started a bev combination trial under the hypothesis that stemness inhibition of cancer cells will sensitize them to chemo and targeted therapies. The safety and efficacy data bodes well for the trial with 609 patients
👍	**Nivo+ipi in dMMR/MSI-H**: The trial evaluates multiple combinations with nivolumab. Absence of new safety findings is encouraging and bodes well for a nivo+ipi combination in a larger Phase III trial
👍	**Reg vs. TAS-102 as salvage**: TAS-102 presents the greatest threat to Bayer´s regorafenib. It was anticipated that TAS-102 will do better for patients with poor PS. In the absence of clear differentiation, Bayer is likely to use its promotional muscle to out-message
👎	**Pembro + mFOLFOX6**: There is some signal of activity in MMR proficient segment indicating a broader utility of the combination. However, the potential of additional toxicity would be a concern
👎	**CORRECT (HFSR with regorafenib)**: This abstract is to associate HFSR incidence with good clinical outcomes. Beyond the fact that HFSR is a known AE for regorafenib, this data is not likely to impact physicians´ treatment decision
👍	**Pembro in pre-treated dMMR CRC:** The readout is very positive specially knowing that the patients were heavily pre-treated. Physicians would be eagerly anticipating a larger trial for validation of these results
👍	**NORDIC 9**: The positive safety of S-1 as mono and in combination with other regimens in old patients, is a great messaging platform that Taiho is likely to leverage in the congress
👎	**Pembro + azacitidine in Pre-treated CRC**: This combination is dead, in all probability given the lack of efficacy
👍	**Fruquintinib (FRESCO)**: Chi-Med and Lilly have been developing fruiquintinb for China and have filed it at CFDA. It remains to be seen if Lilly will use the RECOURSE data for filing with FDA and EMA or initiate a registration study for US and EU
👍	**Ensituximab in refractory CRC**: It would be interesting to find Neogenix Oncology´s future plans. The data certainly looks encouraging
👍	**KEYNOTE-164 and 158**: This analysis confirms pembro´s utility in MSI-H CRC. MSD will message the utility of Pembro as a monotherapy in dMMR/MSI-H CRC across Tx lines
👍	**TAS-102 in OL RWE Study:** Elsevier and Taiho will eagerly promote the real-world confirmation of TAS-102´s registration study

Key Ongoing Trials

👍	**KEYNOTE-177:** This is a highly anticipated trial - that I/O is relevant for dMMR/MSI-H CRC is well understood. Physicians would be curious to understand how to identify the patient as eligible for pembrolizumab. Additionally, the survival outcomes on treatment-beyond-progression would be of high interest as it would allow them to delay chemo as long as feasible
👍	**AVETUX-CRC Trial:** This trial will set the ground for incremental clinical value of avelumab on top of cetuximab+FOLFOX, beyond the biological rationale of CRC tumors becoming immunogenic on being treated with cetuximab and FOLFOX
👍	**Durva + Treme (CCTG CO.26):** This study will test the hypothesis that I/O-I/O combination will benefit CRC irrespective of the MMR proficiency or MSI status
👍	**SCOOP, napabucasin (BBI-608) + pembro:** Boston Biomedical´s strategy is centered on combining napabucasin with maximum number of compounds. This trial is being conducted specifically in 1L refractory patients i.e. patients who haven´t responded or are intolerant of 1L regimens. The expected rationale - the JAK/STAT inhibition is likely to increase the PD-L1 expression which enables pembro to competitively bind with the tumor cells thereby leading to increased recognition by T-cells
👍	**Dose escalation of TAS-102+Oxaliplatin:** This trial is one in the series of TAS-102 combination with the current SoCs in 1L and 2L CRC to improve patient outcomes
👍	**ATOMIC (FOLFOX +/- atezo):** the I/O-chemo hypothesis is being tested in multiple solid tumors. pembro + FOLFOX looks interesting but raises safety concerns. The physicians would be keen to see the safety results from this trial to if atezo would be a safer combination partner, than pembro

RAS TAKEAWAY

At ASCO 2017, the steadily increasing competitive intensity between Lonsurf (TAS-102, Taiho) and Stivarga (regorafenib, Bayer) will be on display. In addition, the I/O agents are reading out both as monotherapy in specific (dMMR/MSI-H) patient segments, as well as in combinations with other cytotoxic and targeted agents in broader patient segments, across treatment lines. Taiho and Elsevier will be communicating significantly on the real-world confirmation of Lonsurf´s **RECOURSE** trial. Bayer will continue to emphasize on the familiarity aspect of regorafenib and also messaging on sequencing regorafenib ahead of Lonsurf. Both BMS, MSD, Roche and Merck KGaA/Pfizer will be setting the expectations for upcoming readouts for their I/O agents. ASCO 2017 will be a balanced representation of *here and now* data and *ongoing trials* whose data is likely to significantly impact clinical practice in treating CRC