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#GU24

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ASCO GU: Do these data change practice?

Key Highlights			Implications
CONTACT-02 Ph 3 EXELIXIS IPSEN	**2L mCRPC** **Cabozantinib (C)** (TKI) **+ atezolizumab (A)** (anti-PD-L1) ***vs* second NHT** (N=507)	First results from this trial showed statistically significant PFS (6.3m vs 4.2m, HR of 0.65 [95% CI: 0.50 - 0.81]; *P*=0.0007) in post-NHT pts (only 23% had prior chemo). No OS benefit yet (HR: 0.79 95% CI: 0.58 - 1.07, *P*=0.13) but data were immature. Gr 3/4 AEs reported, 33% vs 8%	OLs criticized the control arm for having a NHT switch (2nd NHT) and the trial did not allow chemo in control arm. PFS diff were also said to appear modest. Less promising OS curves, additional toxicity and cost were other key comments, while the mature OS data are awaited
BRCAAway Ph 2 **Institutional sponsored**	**1L mCRPC BRCA/ATM** Arm 1: **AAP** (NHT) Arm 2: **Olaparib** (PARPi) vs Arm 3: **AAP + Olaparib** (N= 165)	Combination of ARPI and PARPi has shown highest PFS benefit (39m vs 14m) with HR of 0.32 (95% CI: 0.14-0.75) vs olaparib alone. Significant PFS benefit (39m vs 8.4m) with HR of 0.28 (95% CI: 0.13-0.65) vs abiraterone alone	1L NHT + PARPi showed superior PFS vs PARPi alone in BRCA1/2 & ATM pts. It further supports usage of this regimen in 1L HRRm setting. AZ's olaparib + AAP, Pfizer's talazoparib + enza, JNJ's niraparib + AAP are approved regimens in the US & EU for 1L mCRPC
EMBARK Ph 3 Pfizer	**High risk BCR PC** **Enza mono** (NHT) vs **Leuprolide** (ADT) **+** placebo (N = 713)	At week 37 (if PSA <0.2 ng/ml), more pts with enzalutamide mono (86%) had tx suspension vs leuprolide (67%). Among pts with tx suspension, no difference in MFS observed between the arms. But MFS was superior if tx was not suspended (although in small pt numbers)	Pfizer's enzalutamide +/- ADT has been approved for high-risk BCR patients. Current result suggests that suspension of enza monotherapy (after PSA respons to undetectable level) may be associated with lower MFS benefits vs ADT. But OS data are awaited
CYPIDES Ph 2 MERCK ORION PHARMA	**mCRPC AR mut** **MK-5684/ ODM-208 mono** (CYP11A1i) (N=134)	Additional results showed 56% PSA50 in AR-LBD mut and 17% in AR wild type. ORR 20.5% for AR-LBD positive. Gr ≥ 3 AEs in 47.8% of patients	MK-5684 continues to show promising response in AR-LBDmut pts while results appear modest in AR-wild type group. Two Ph 3 trials ongoing in post-NHT & chemo mCRPC (includes both AR-LBD positive & negative pts)
UNITE **Institutional sponsored**	**Adv. mUC** **Enfortumab vedotin** (anti-Nectin 4 ADC) after upfront platinum chemo + Avelumab maintenance (N=49)	At a median follow-up of 8.5 months from start of enfortumab vedotin (EV), the retrospective analysis showed that ORR was 55%. mPFS and mOS were 7 and 13.3 months, respectively	Results suggest that EV appears to benefit mUC patients who had sequential platinum-based chemo & avelumab maintenance EV-301 Ph 3 trial, that supported full approval in the US, did not include avelumab-progressed patients
AMBASSADOR Ph 3 MERCK NIH NATIONAL CANCER INSTITUTE	**Adj MIBC** **Pembrolizumab** (anti-PD-1) ***vs* Observation** (N=702)	First results from this trial showed significant mDFS benefit (29m vs 14m) in pembro arm compared to observation arm with HR of 0.69 (95% CI 0.55–0.87 p=0.0013). But, no OS benefit (50.9m vs 55.8m) with HR of 0.98 (95% CI 0.76–1.26 p=0.88). Gr >3 AEs 48.4% vs 31.8%	DFS looks similar to BMS' nivolumab (HR:0.71), the only approved anti-PD-1 in MIBC. Similar to historical trials, results validate DFS benefit but showed no OS benefit yet. Final OS results awaited. If approved, pembro may become an additional option for these patients
KEYNOTE-564 Ph 3 MERCK	**Adj ccRCC** **Pembrolizumab** (anti-PD-1) ***vs* Placebo** (N=994)	Trial showed statistical significant OS with pembro compared vs placebo (HR: 0.62, 95% CI 0.44 - 0.87; P=.002; 2 yr OS rate: 91.2% vs 86%). DFS benefit was consistent with prior interim analyses with HR 0.72 (95% CI 0.59 - 0.87)	KN-564 reportedly the first trial to show OS benefit with adjuvant therapy in RCC. In Nov 2021, adj. pembro was approved. It has already become a SoC for RCC patients at intermediate-high or high-risk recurrence following surgery. The positive OS may reaffirm its utility in this setting
CheckMate 9ER Ph 3 EXELIXIS Bristol Myers Squibb	**1L Adv. ccRCC** **Nivolumab** (anti-PD-1) **+ cabozantinib** (anti-TKI) vs **Sunitinib** (anti-RTK) (N=323)	After 4 year follow-up, results showed significant OS benefit (46.5m vs 36m, HR 0.77 [95% CI 0.63 - 0.95]. Gr ≥ 3 TRAEs were 67.5% vs 55.3%	Long term OS benefit supports current usage of I/O + TKI (1L nivolumab + cabo) as a SoC in untreated ccRCC

Potentially may become SoC | Practice assuring results | Further results needed for clinical utilization | May remain as additional option