

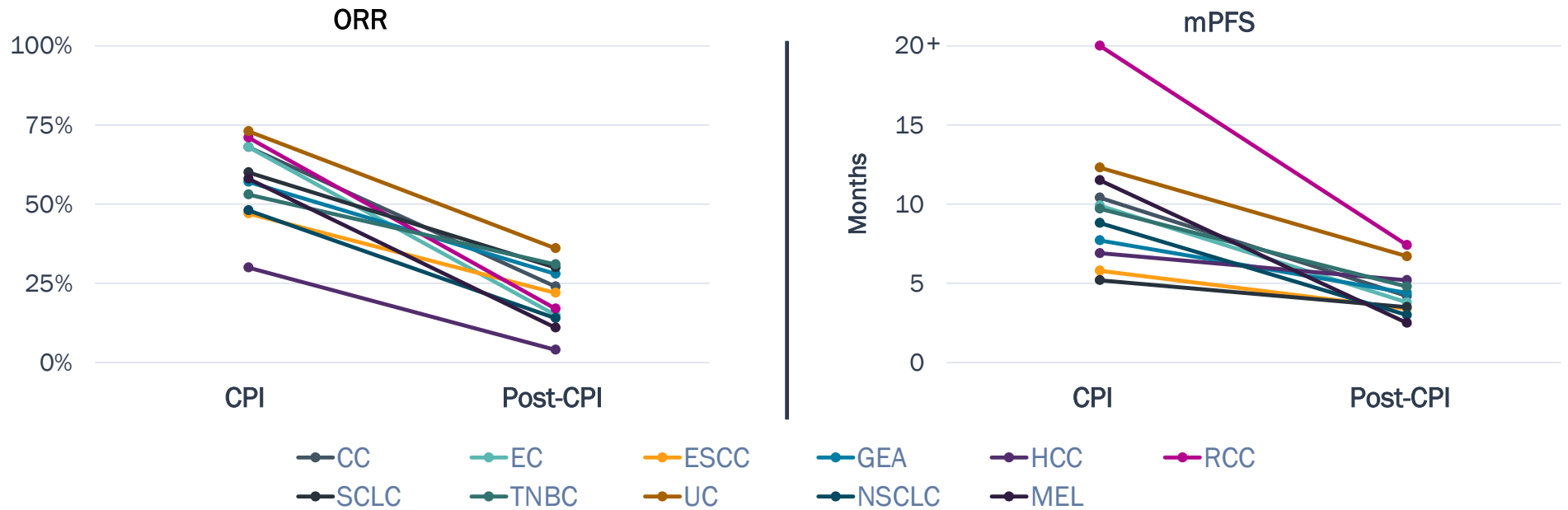
Oncology Pulse

Overcoming PD-(L)1 Resistance

September 2023

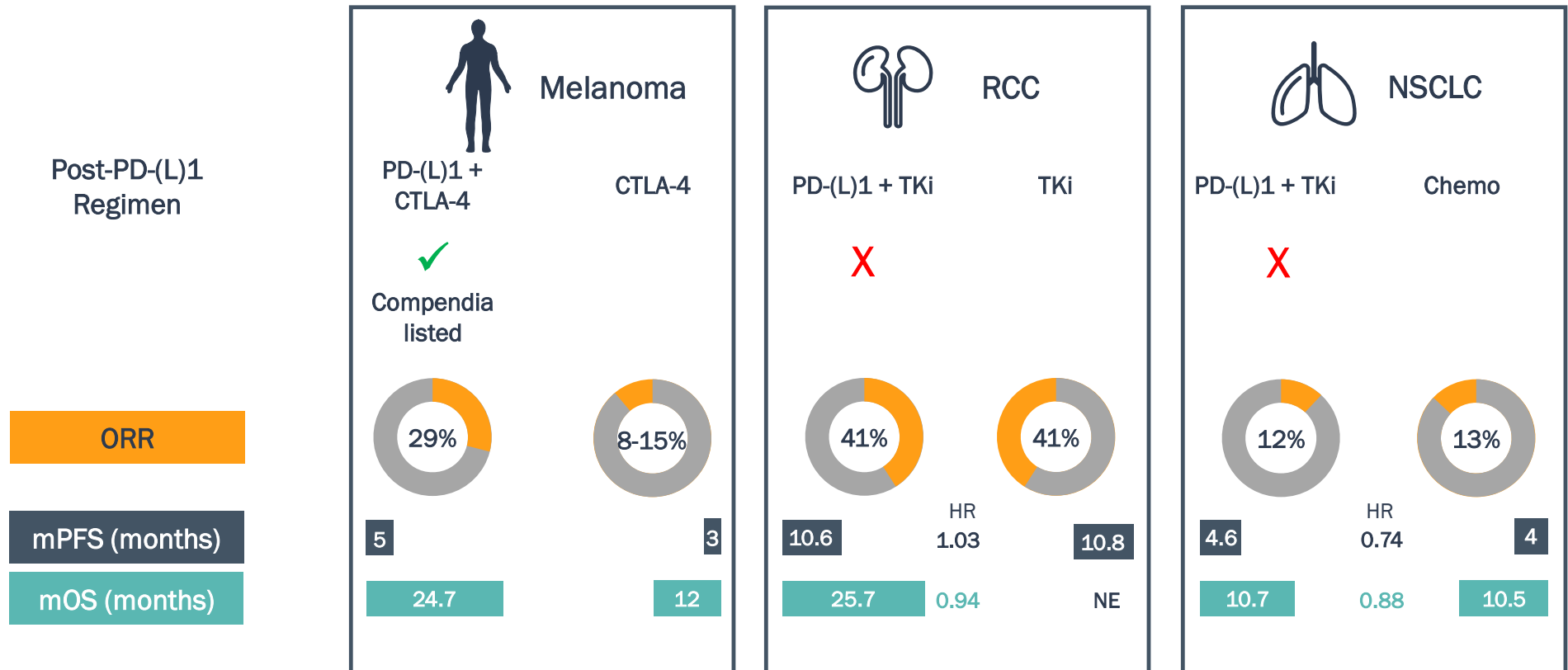
1L checkpoint inhibitor approvals have improved efficacy for many solid tumors and also widened the gap between 1L and 2L SoC

Efficacy of 1L and 2L in Solid Tumors with 1L PD-(L)1 Approvals



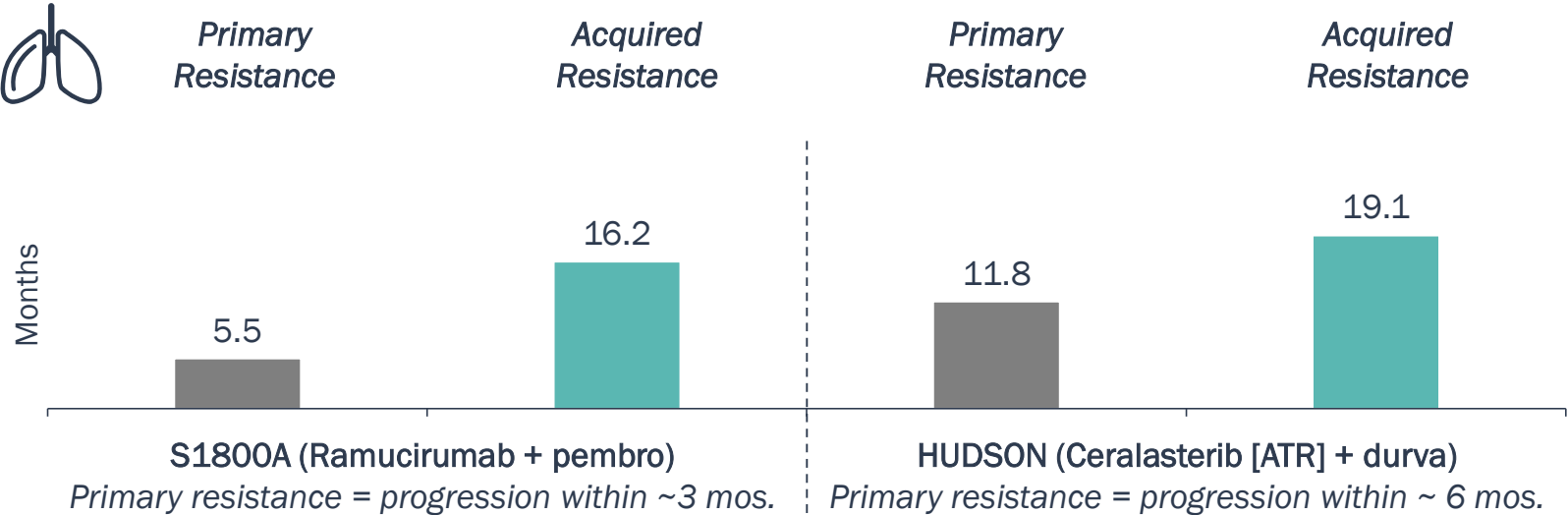
Despite some promising early results, Phase 3 trials investigating PD-(L)1 re-challenge have only succeeded in melanoma

Successes and Failures of CPI Rechallenge in Prospective Studies

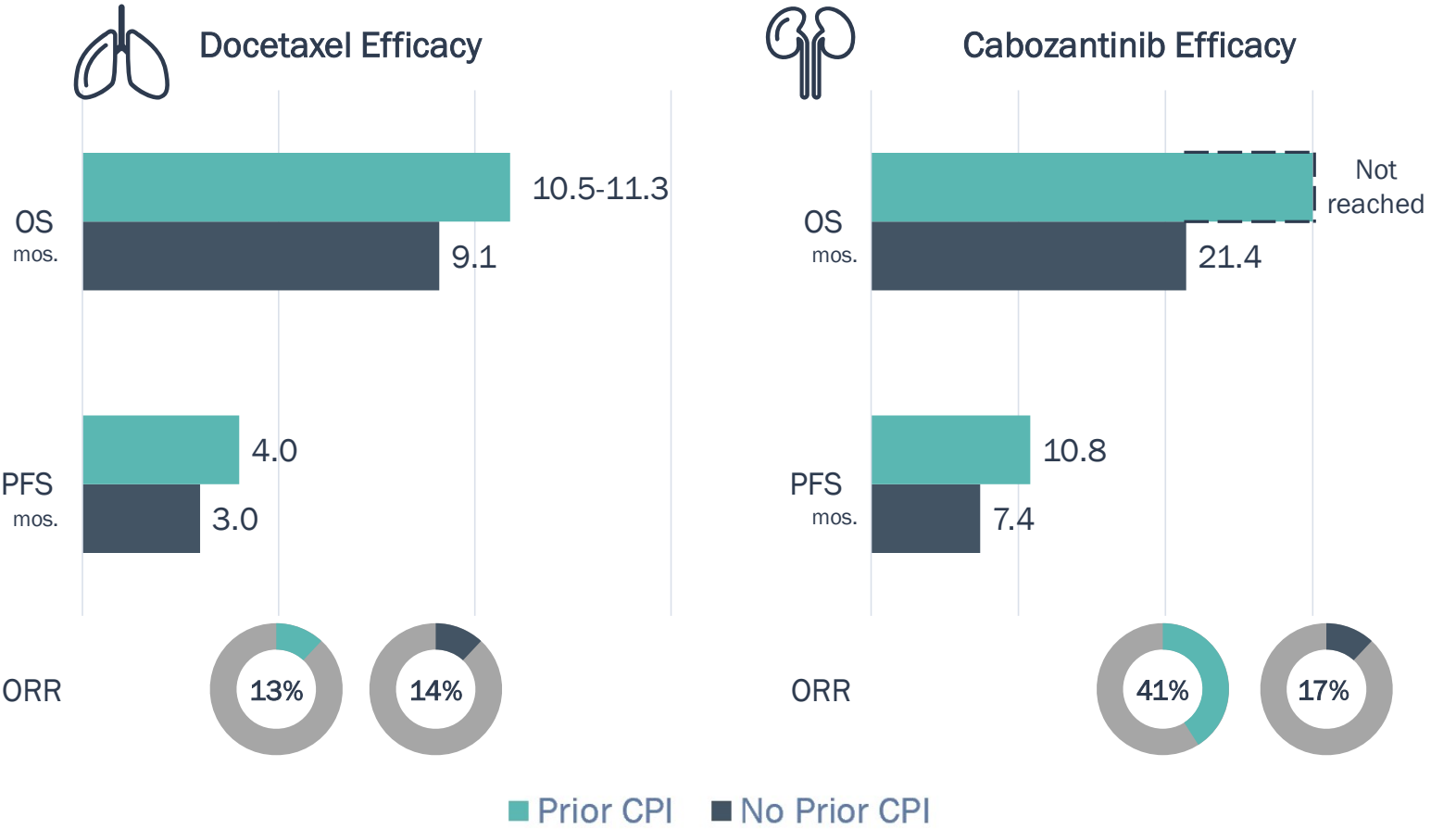


Data from NSCLC trials suggests efficacy may be limited to patients with acquired, rather than primary, CPI resistance

Median Overall Survival (mOS) by Type of Resistance



In addition, control arms from these trials suggest that CPI may impact the efficacy of subsequent therapies, particularly in RCC



Are pending rechallenge Ph3 trials in NSCLC likely to produce different results?

Optimism is higher for SWOG's trial that selects for patients with prior PD-(L)1 benefit
 Pending Pivotal PD-(L)1 Retreatment Trials – NSCLC



Trial	Sponsor	Est. PCD	Regimen	Criteria for Prior PD-(L)1
Ph3: LEAP-008	MERCK Eisai	Aug 2023	Lenvatinib +/- pembro vs. docetaxel	<ul style="list-style-type: none"> Progressed on or after platinum chemo and one prior anti-PD-(L)1 therapy
Ph3: SAFFRON-301	BeiGene	Jun 2024	Sitravatinib [multi-TKI] + tislelizumab vs. docetaxel	<ul style="list-style-type: none"> Progressed on or after one prior anti-PD-(L)1 therapy
Ph3: PRAGMATICA-LUNG	SWOG CANCER RESEARCH NETWORK	Mar 2025	Ramucirumab + pembro vs. standard of care chemo	<ul style="list-style-type: none"> Must have had a best response on anti-PD-(L)1 of SD, PR or CR
Ph3: LATIFY	AstraZeneca	May 2025	Ceralasertib [ATR] + durva vs. docetaxel	<ul style="list-style-type: none"> Documented PD on or after most recent treatment regimen
Ph2/3: COSTAR Lung	gsk	Jan 2026	Cobolimab [TIM-3] + dostarlimab + docetaxel vs. dostar + docetaxel vs. docetaxel	<ul style="list-style-type: none"> Progressed on or after one prior anti-PD-(L)1 therapy

Failed
Sep 2023

Similar to failed
Sapphire trial

Since our last Pulse, 6 new oncology agents have been approved (including 4 bispecifics for heme indications)

	Targeted	Cell/Gene Therapy	IO	Bispecific	ADC	Other	Radiopharm
Approved	Jaypirca (BTK) ^{AA} Vanflyta (FLT3) Ojjaara (JAK)	Omisurge (enhanced CD34+ stem cells)	Zynyz (PD-1)	Epkinly (CD20xCD3) ^{AA} Columvi (CD20xCD3) ^{AA} Talvey (GPRC5DxCD3) ^{AA} Elrexio (BCMAxCD3) ^{AA}		Orserdu (SERD)	
Filed	Nirogacestat (γ secretase) Fruquitinib (VEGF) Repotrectinib (ROS1) Capivasertib (AKT) Zolbetuximab (claudin18.2) Rivoceranib (VEGF) Imetelstat (telomerase) Tovorafenib (panRAF) Apatinib (VEGF)	Lifileucel (TILs) Afimi-cel (MAGEA4)²	Penpulimab (PD-1) Cosibelimab (PD-L1) Camrelizumab (PD-1) Tislelizumab (PD-1) Torapalimab (PD-1)				
On Deck	Axatilimab (CSF1R)	Tabelecleucel (T cells) (filed in EU)					Iomab-B (CD45)
Rejected	Hypericin (PDT ¹)		ALT-803 (IL-15)		Trastuzumab duocarmazine (HER2)		

Bold = novel target; Approved since May 2023

1 PDT = photodynamic therapy 2 rolling BLA initiated

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