SITC 21
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Clinical Activity of ICT01, an anti-BTN3A-Targeted, γ9δ2 T Cell-Activating mAb, Alone and in Combination with Pembrolizumab in Patients with Advanced Solid Tumors: EVICTION Trial

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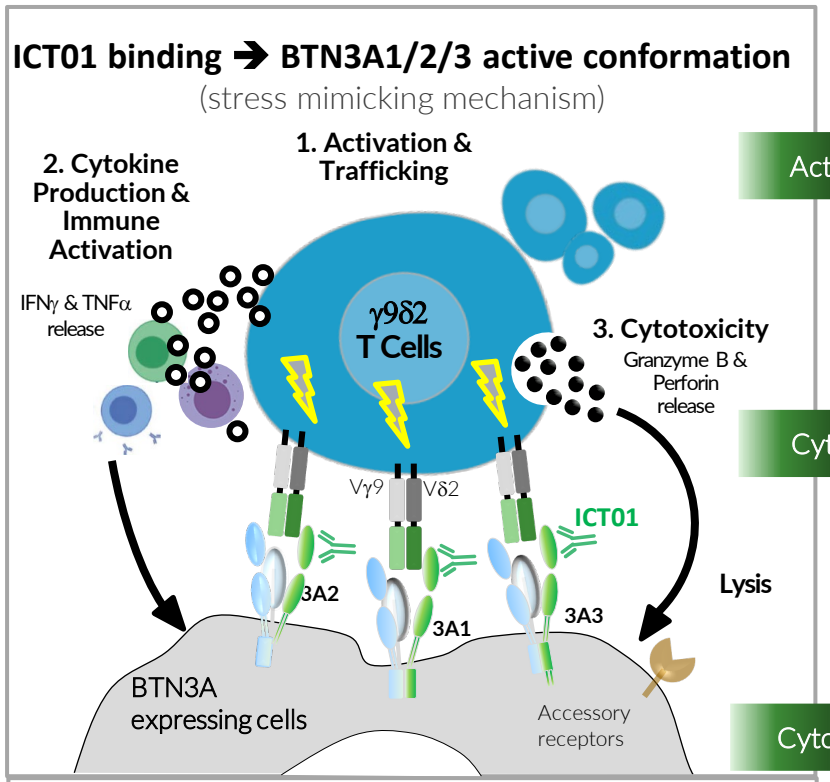
Disclosures

Company Name	Relationship	Self/Family	
Novartis	Consulting Fee (e.g. advisory boards)	Self	⊗
Immatics	Consulting Fee (e.g. advisory boards)	Self	⊗
Roche	Consulting Fee (e.g. advisory boards)	Self	⊗
Roche	Contracted Research	Self	⊗
Bristol Myers Squibb	Consulting Fee (e.g. advisory boards)	Self	⊗
Pfizer	Consulting Fee (e.g. advisory boards)	Self	⊗
Gemoab	Consulting Fee (e.g. advisory boards)	Self	⊗
MSD	Consulting Fee (e.g. advisory boards)	Self	⊗
AstraZeneca	Consulting Fee (e.g. advisory boards)	Self	⊗
Lilly	Consulting Fee (e.g. advisory boards)	Self	⊗
Boehringer Ingelheim	Consulting Fee (e.g. advisory boards)	Self	⊗

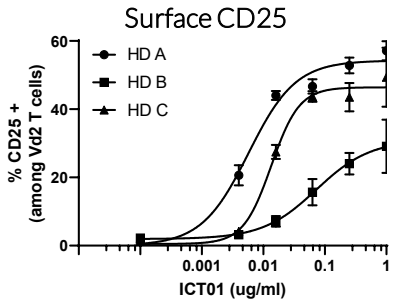
The EVICTION trial is fully sponsored by ImCheck Therapeutics

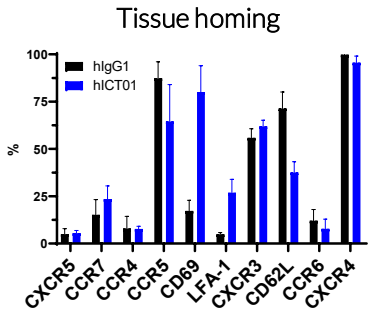
ICT01: a First-in-Class anti-BTN3A that Selectively Activates the Anti-Tumor Repertoire of γ9δ2 T Cells



1. Activation & trafficking from the blood in <30 min
2. Cytokines lead to recruitment of other immune cells, including NK cells, CD8 T cells and B cells
3. Cytotoxicity requires a 2nd confirmatory signal (e.g., NKG2D-MICA) to allow activated γ9δ2 T cells to kill stressed/malignant/infected cells and sparing healthy cells expressing BTN3A.

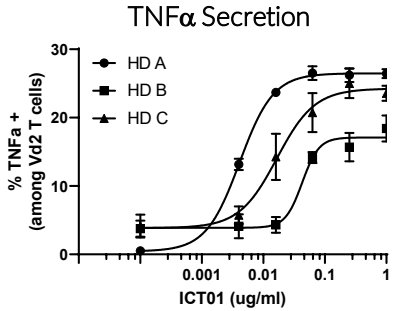
Activation

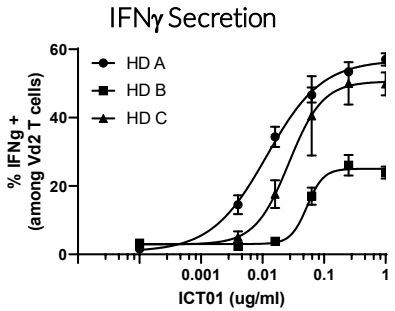




Migration into tumors

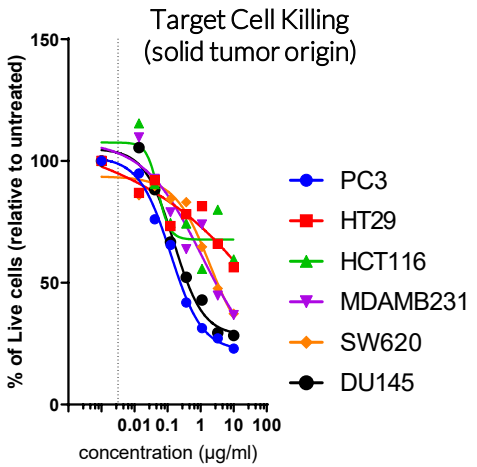
Cytokines

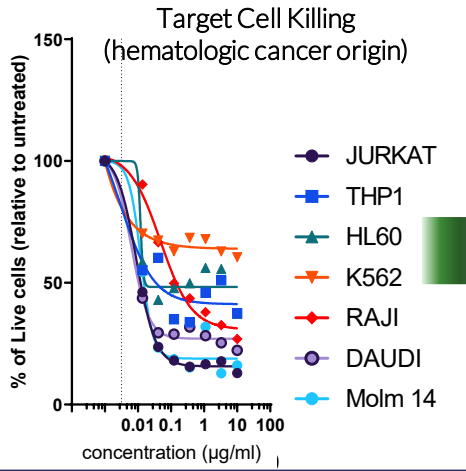




Expanded immune response & remodeling of TME

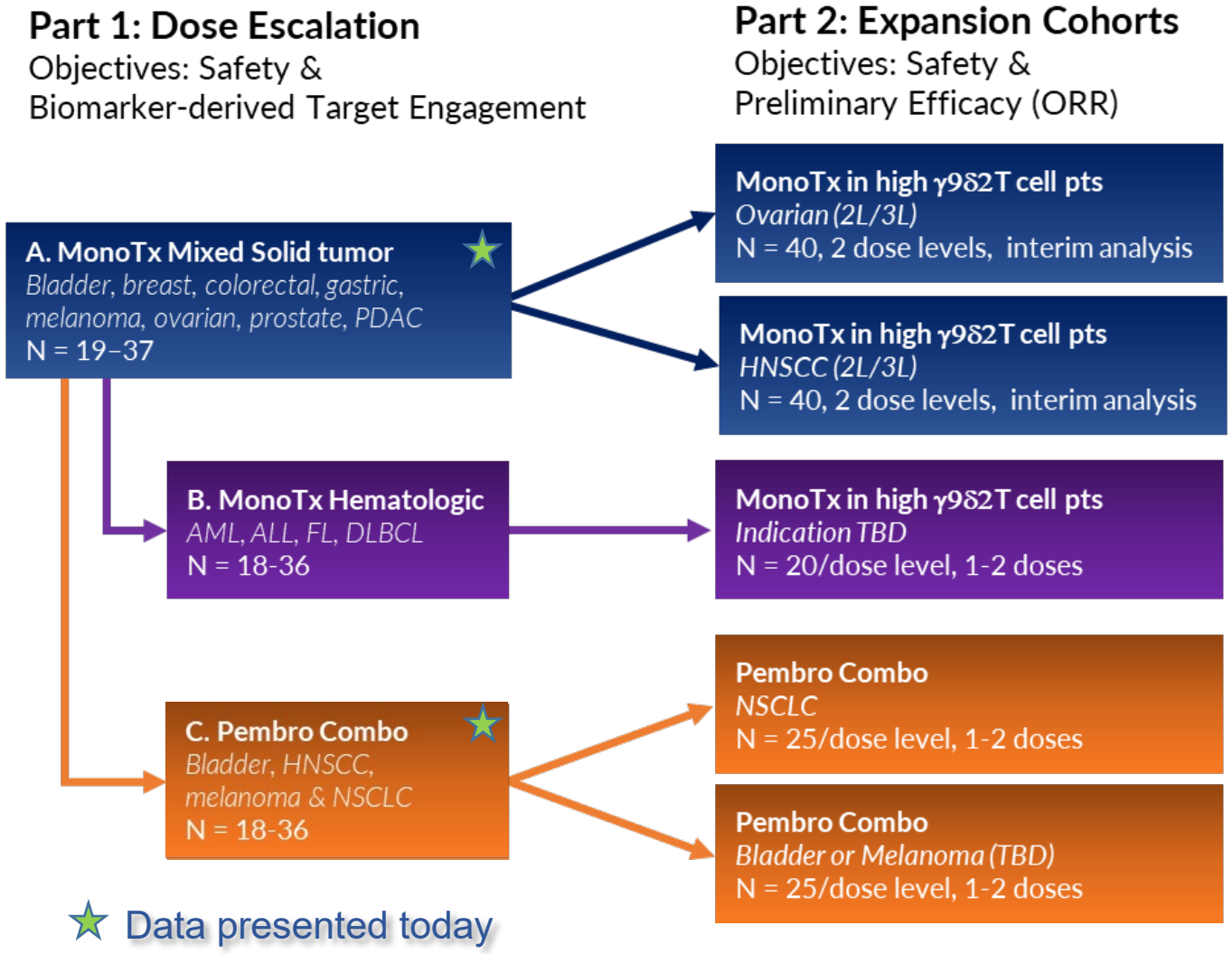
Cytotoxicity





Selective killing of malignant cells

EVICTION Trial Design: ICT01 as Monotherapy and in Combination with Pembrolizumab in Patients with Advanced, R/R Cancer



Part 1 Basket Indications:

1. BTN3A-expressing tumors
2. γδ T cell-infiltrating tumors

Part 1 Main Eligibility Criteria:

1. M/F >18 yrs of age
2. No remaining standard of care
3. ECOG ≤ 1
4. Life expectancy > 3 mos
5. Willing to undergo biopsies
6. Pembro combo: failed ≥1 CPI & eligible per approved label

Participating Countries:

France, Belgium, Germany, Spain, UK and US

ICT01 Safety & Tolerability: *No DLTs or Safety Signals Observed to Date*

Common (>1 pt) Related Treatment Emergent AEs by Group and Dose Cohort

Group A Preferred Term[2]	20-700 µg (N=6) n (%)	2 mg (N=5) n (%)	7 mg (N=4) n (%)	20 mg (N=5) n (%)	75 mg (N=7) n (%)	200 mg (N=6) n (%)	Overall (N=33) n (%)
Pyrexia	2 (33%)	3 (60%)	0	4 (80%)	7 (100%)	2 (33%)	17 (52%)
Chills	0	1 (20%)	0	1 (20%)	5 (71%)	2 (33%)	9 (27%)
Asthenia	0	0	3 (75%)	0	2 (29%)	1 (17%)	6 (18%)
Arthralgia	2 (33%)	0	1 (25%)	0	0	2 (33%)	5 (15%)
Nausea	0	0	1 (25%)	2 (40%)	1 (14%)	1 (17%)	5 (15%)
Vomiting	0	0	1 (25%)	2 (40%)	0	1 (17%)	4 (12%)
Fatigue	1 (17%)	0	0	0	1 (14%)	1 (17%)	3 (9%)
Hypotension	0	0	0	2 (40%)	0	0	2 (6%)
Infusion-related reaction	1 (17%)	0	0	0	0	1 (17%)	2 (6%)
Anaemia	1 (17%)	1 (20%)	0	0	0	0	2 (6%)
Diarrhoea	0	0	0	1 (20%)	1 (14%)	0	2 (6%)
Rash	0	0	0	1 (20%)	1 (14%)	0	2 (6%)

Group B Preferred Term	200 µg (N=3)	700 µg (N=3)	2 mg (N=3)	7 mg (N=3)	20 mg Enrolling	75 mg Planned		Overall (N=12)
Pyrexia	0	1 (33%)	1 (33%)	1 (33%)		NA	NA	3 (25%) 4
Vomiting	0	1 (33%)	1 (33%)	0		NA	NA	2 (17%) 2

Group C Preferred Term	700 µg (N=4)	2 mg (N=4)	7 mg (N=4)	20 mg (N=?)	75 mg Enrolling	200 mg Planned	Overall (N=11)*
Asthenia	1 (25%)	1 (25%)	0		NA	NA	2 (18%) 2
Pyrexia	0	1 (25%) 1	1 (25%) 1		NA	NA	2 (18%) 2

Summary:

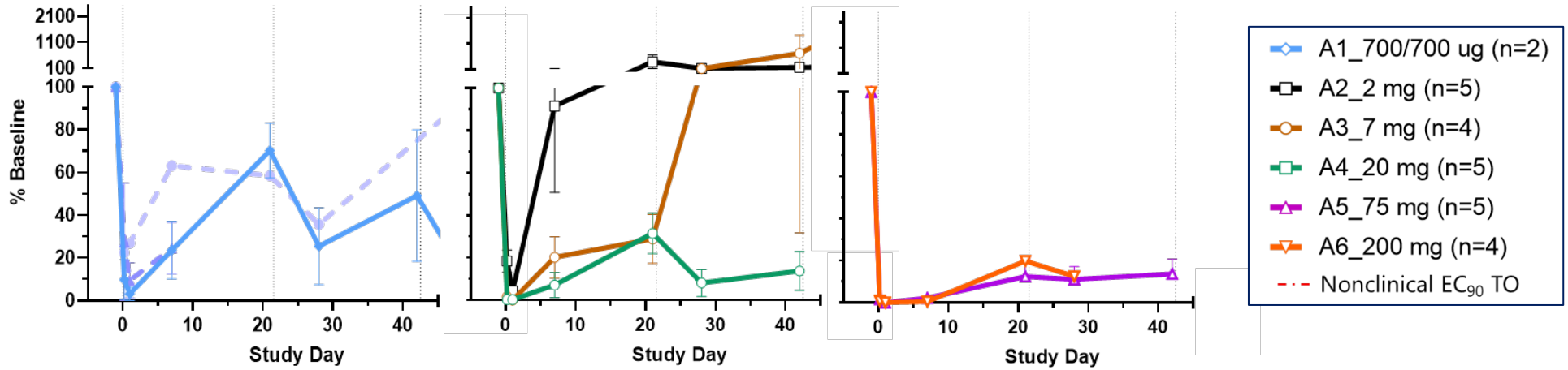
1. First-dose fever & chills are most common AEs
2. No change in severity with dose (Grade 1/2), but more frequent
3. Rarely recurs (1/32 pts in Group A) with subsequent doses
4. Likely cytokine-mediated and characterized as an IRR or CRS

[1] Events considered related to study drug include those reported with a causality to ICT01 of 'Possible', 'Probable' or 'Related'. Patients reporting an adverse event more than once are counted only once.
[2] Adverse events are coded to preferred term using MedDRA, version 23.1.
*One pt was dose escalated from 700 µg to 2mg so is counted in the AE colums for both doses

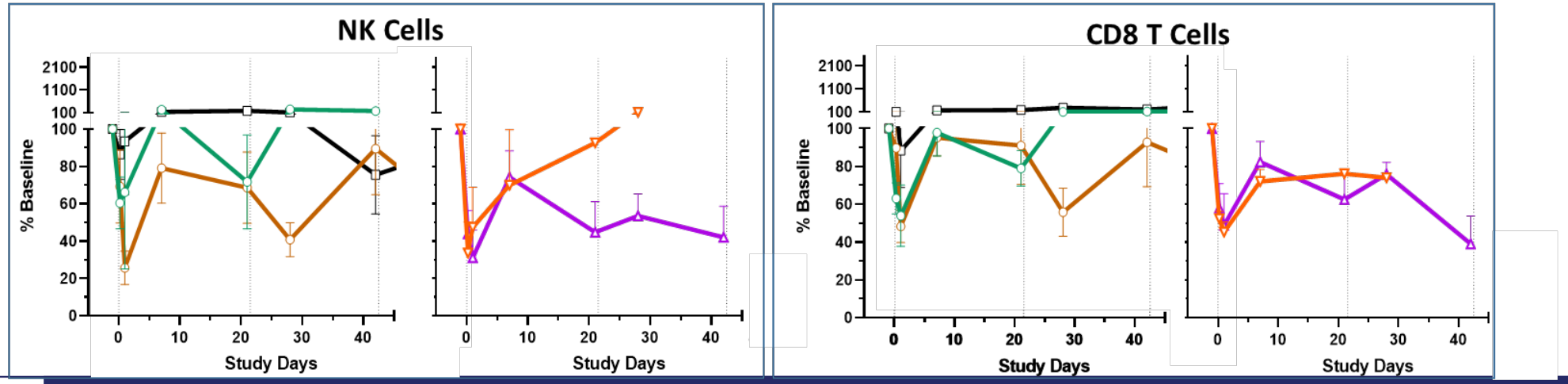
Re-Distribution of Multiple Immune Cell Subsets post ICT01 (Group A)

Dose-Dependent Migration of γ9δ2 T Cells from the Circulation

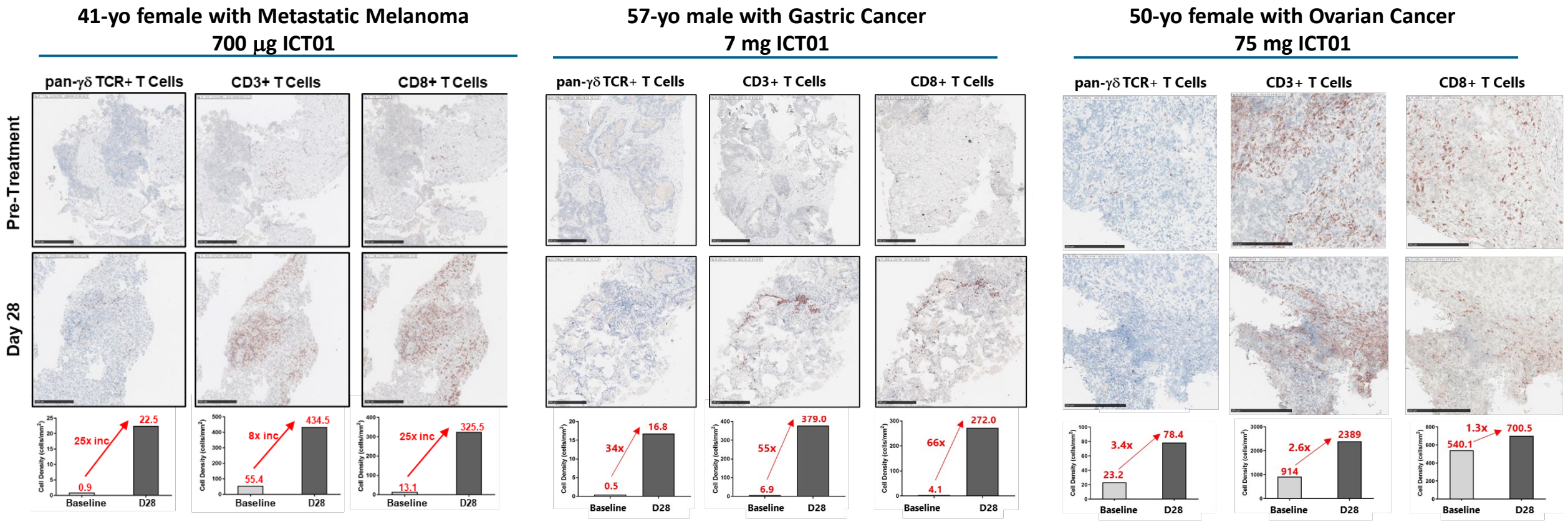
Doses as low as 700 mcg induce migration of all circulating γ9δ2 T cells



ICT01 Doses ≥ 7 mg Induce Migration of NK and CD8 T Cells

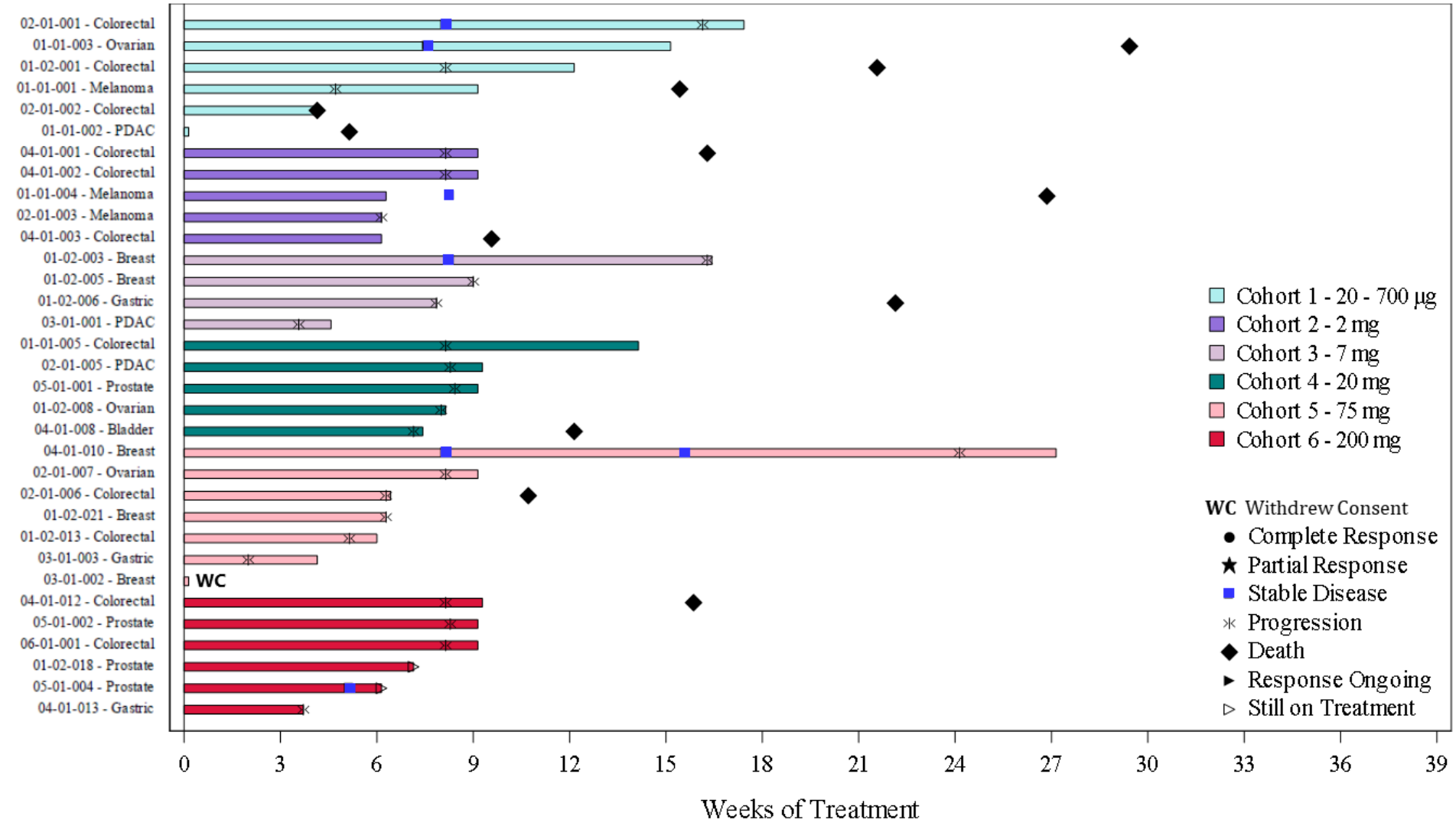


ICT01 Increases Tumor Infiltration of γδ, CD3 and CD8 T Cells



Digital Pathology: automated cell counts per mm² of tumor (HalioDx)

ICT01 Monotherapy Swimmer Plot: RECIST1.1 Performed Every 8 Weeks

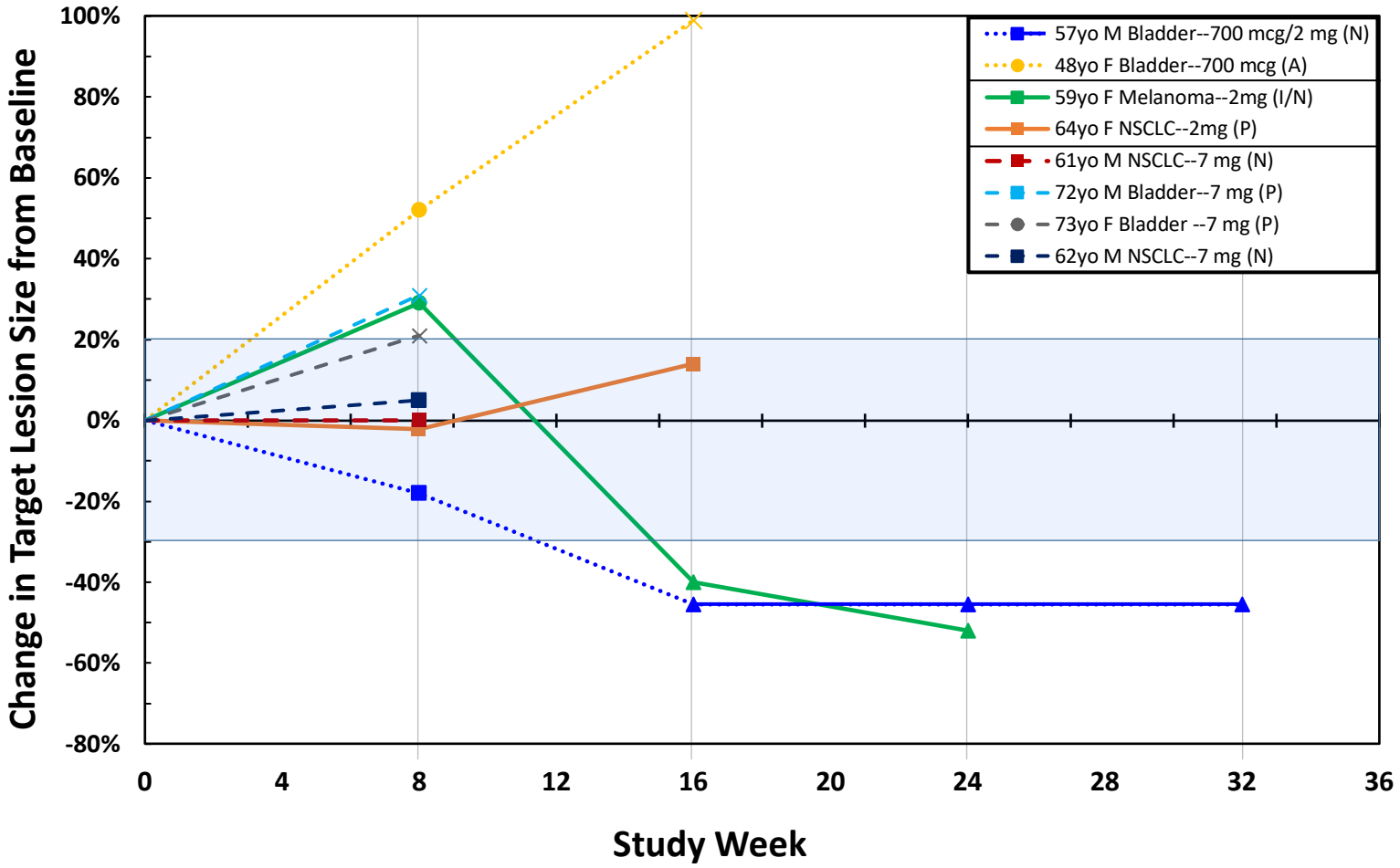


Efficacy evaluable:

SD in 6 of 19 pts

- 2 Breast
- 1 CRC
- 1 Ovarian
- 1 Melanoma
- 1 Prostate

Spider Plot of CPI-Refractory Solid Tumor Patients: ICT01 + Pembro 200mg Q3W



ICT01 Dose Cohorts:

700 mcg (n=2*)
2 mg (n=2+)
7 mg (n=4+)

*1 pt died of a stroke Wk 4; not efficacy evaluable
+1 pt in each cohort was not efficacy evaluable due to an underdosing error (~1/10th the dose)

Key

Prior CPI Therapy:
A, avelumab
I, ipilimumab
N, nivolumab
P, pembro

Response:
○ = iUPD
□ = SD
△ = PR
X = PD/Off study

Efficacy Evaluate Objective Response Rate 2/8 = 25%
Efficacy Evaluable Disease Control Rate 5/8 = 62%

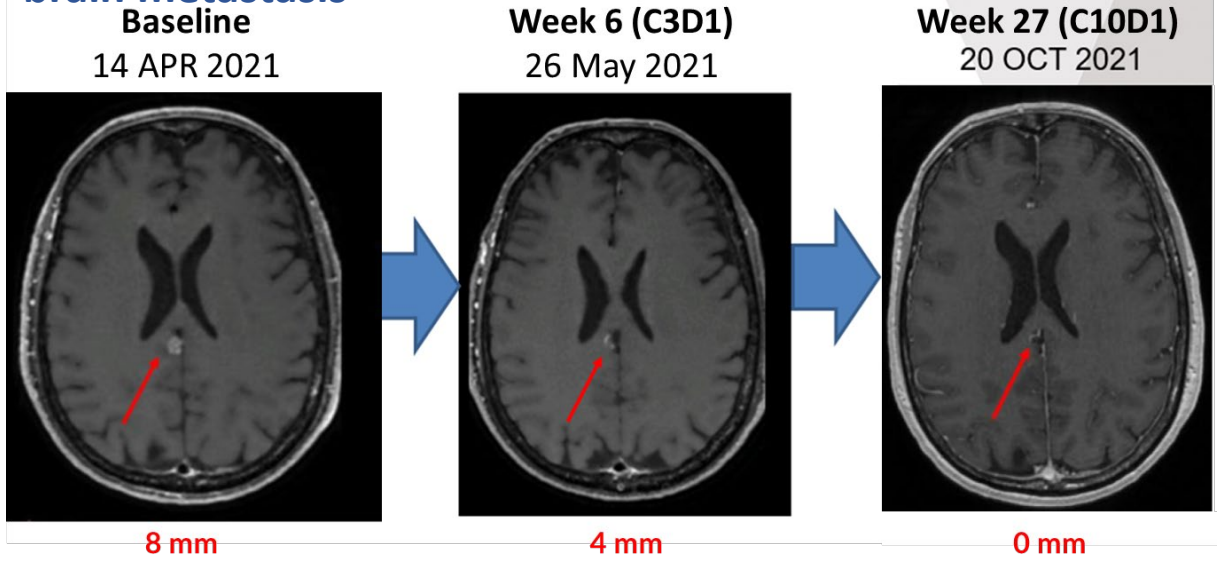
Summary of a 59-yo Female with Ipi/Nivo Refractory Metastatic Melanoma

Complete Response of Brain Metastasis and Partial Response of Liver Metastasis

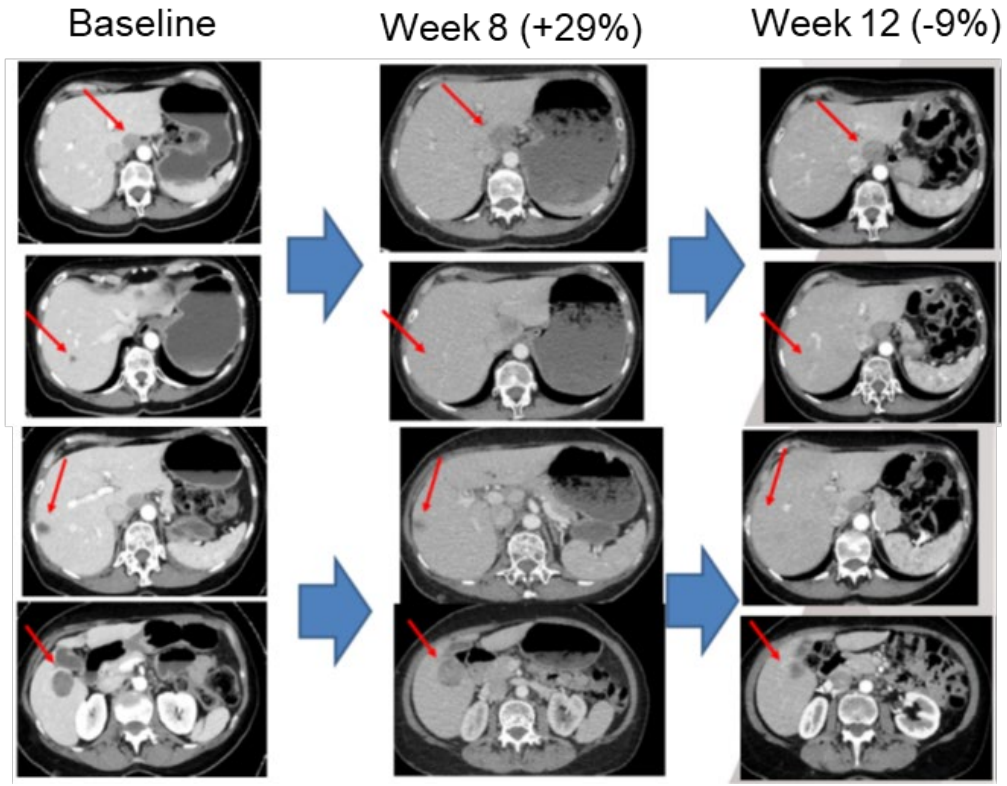
GUSTAVE ROUSSY CANCER CAMPUS GRAND PARIS | DITEP Drug Development Department

Pt 01-01-007 EVICTION Group C ICT01 2mg + pembro combo
59 yo female treated for metastatic melanoma (BRAF wt)
with CNS and liver mets NIVO + IPI refractory
C1D1 14 APR 2021

Asymptomatic brain metastasis



Target Lesions in Liver



Summary of Tumor Imaging:

1. CR of brain lesion is encouraging and requires study of additional patients with brain metastases.
2. Pseudoprogression in liver at Week 8 followed by improvement (Wk 16 -40% and Wk 24 -52% by RECIST) is consistent with other immunotherapies.

Summary of EVICTION Trial Results to date

ICT01 Monotherapy

1. Safety and tolerability: escalation to maximum planned dose with no DLTs or safety concerns
2. PD effects: activation and migration of γ9δ2 T cells, increases in serum cytokines correlated with activation of NK, CD8 T cells, and granulocytes, with a resultant increase in tumor-infiltration of γδ, CD3 and CD8 T cells that are linked to baseline γ9δ2 T cell counts.
3. Phase 2a: Cohort Expansion in 2L/3L Ovarian and HNSCC patients with high baseline γ9δ2 T cells (≥ 20K/mL blood) initiated Q4 2021.

ICT01 plus Pembrolizumab

1. Dose escalation ongoing with no DLTs observed up to 20 mg ICT01 + 200 mg Pembro.
2. Preliminary signs of tumor regression observed at low ICT01 doses likely reflect the contribution of remodeling of the tumor immune microenvironment by ICT01 and activation of CD8 T cells by pembrolizumab.
3. Additional experience with the combination needed to confirm these results with expansion cohorts expected to initiate in 2022.