PARIS 2022 ESMO congress

The Combination of ICT01, a γ9δ2 T Cell-activating mAb, plus Pembrolizumab Induces a Broad Antitumor Immune Response and Disease Control in Patients with CPI-Failure Melanoma, NSCLC and Bladder Cancer: The EVICTION Trial

Abstract 732MO

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DECLARATION OF INTERESTS

Stéphane Champiat

Honoraria: Amgen, Astellas, AstraZeneca, Bristol Myers Squibb, Eisai, Genmab, Janssen, Merck, Novartis and Roche.

Principal Investigator of Clinical Trials for: Abbvie, Amgen, Cytovation, Eisai, Imcheck Therapeutics, Molecular Partners Ag, Merck, Ose Pharma, Pierre Fabre, Sanofi Aventis, Sotio A.S, Transgene

Advisory Board/Consulting: Alderaan Biotechnology, Amgen, AstraZeneca, Avacta, Celanese, Ellipses Pharma, Immunicom, Inc., Nanobiotix, Oncovita, Pierre Fabre, Seagen, Tatum Bioscience, Tollys SAS, UltraHuman8

Travel and congress: Amgen, AstraZeneca, Bristol Myers Squibb, Merck, Ose Pharma, Roche, Sotio

As part of the Drug Development Department (DITEP) =

Principal/sub-Investigator of Clinical Trials for Abbvie, Adaptimmune, Adlai Nortye USA Inc, Aduro Biotech, Agios Pharmaceuticals, Amgen, Astex Pharmaceuticals, Astra Zeneca Ab, Aveo, Basilea Pharmaceutica International Ltd, Bayer Healthcare Ag, Bbb Technologies Bv, Beigene, BicycleTx Ltd, Blueprint Medicines, Boehringer Ingelheim, Boston Pharmaceuticals, Bristol Myers Squibb, Ca, Casi Pharmaceuticals, Inc, Celgene Corporation, Cellcentric, Chugai Pharmaceutical Co, Cullinan-Apollo, Curevarc, Daiichi Sankyo, Debiopharm, Eisai, Eisai Limited, Eli Lilly, Exelixis, Faron Pharmaceuticals Ltd, Forma Tharapeutics, Gamamabs, Genentech, Glaxosmithkline, H3 Biomedicine, Hoffmann La Roche Ag, Imcheck Therapeutics, Incyte Corporation, Innate Pharma, Institut De Recherche Pierre Fabre, Iris Servier, Iteos Belgium SA, Janssen Cilag, Janssen Research Foundation, Janssen R&D LLC, Kura Oncology, Kyowa Kirin Pharm. Dev, Lilly France, Loxo Oncology, Medimmune, Menarini Ricerche, Merck Sharp & Dohme Chibret, Merrimack Pharmaceuticals, Merus, Molecular Partners Ag, Nanobiotix, Nektar Therapeutics, Novartis Pharma, Octimet Oncology Nv, Oncoethix, Oncopeptides, Orion Pharma, Genomics, Ose Pharma, Pfizer, Pharma Mar, Pierre Fabre Medicament, Relay Therapeutics, Inc, Roche, Sanofi Aventis, Seattle Genetics, Sotio A.S, Syros Pharmaceuticals, Taiho Pharma, Tesaro, Transgene S.A, Turning Point Therapeutics, Xencor

Research Grants from Astrazeneca, BMS, Boehringer Ingelheim, GSK, INCA, Janssen Cilag, Merck, Pfizer, Roche, Sanofi

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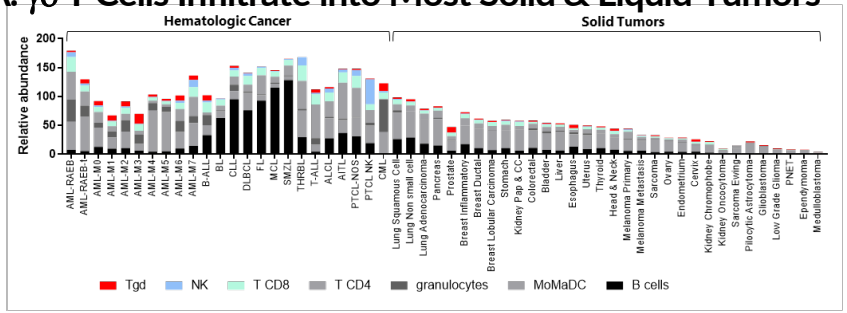
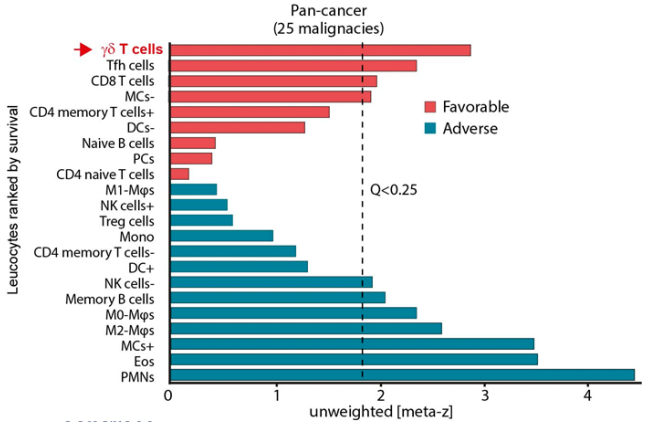
The Rationale & Mechanism of Action of ICT01 to Selectively Activate the Anti-Tumor Potential of γ9δ2 T Cells in Patients with Solid Tumors

A. γδ T Cells Infiltrate into Most Solid & Liquid Tumors

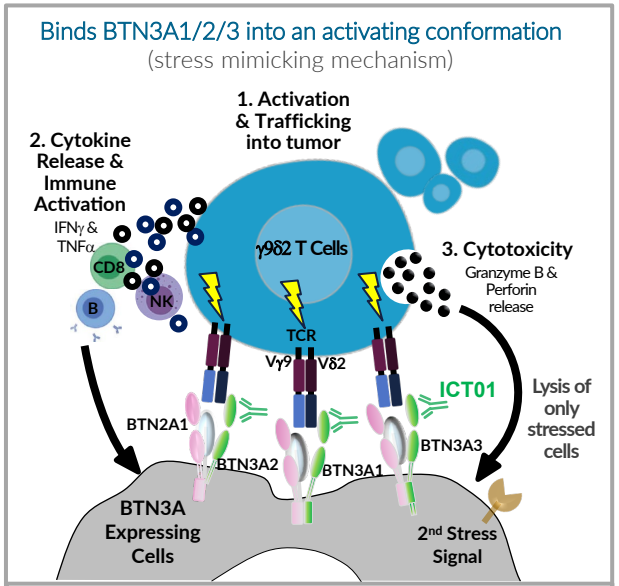


B. Strongest Correlation with Favorable Prognosis of all TILs



Adapted from Tosolini et al, OncoImmunol, 2017 and Gentles et al, Nat Med, 2015

C. ICT01 MOA



- γ9δ2 T cell activation & trafficking in patients in <30 min
2. Cytokines lead to activation of other immune cells, incl T Cells, NKs, APCs & B cells
3. Killing requires 2nd signal (e.g., NKG2D-MICA) to activated γ9δ2 T cells from stressed/malignant/infected cells

EVICTION: Open-label, Phase I/IIa Study of ICT01 Alone and in Combination with Pembrolizumab 200 mg Q3W

Phase 1: Dose Escalation ICT01 IV Q3W

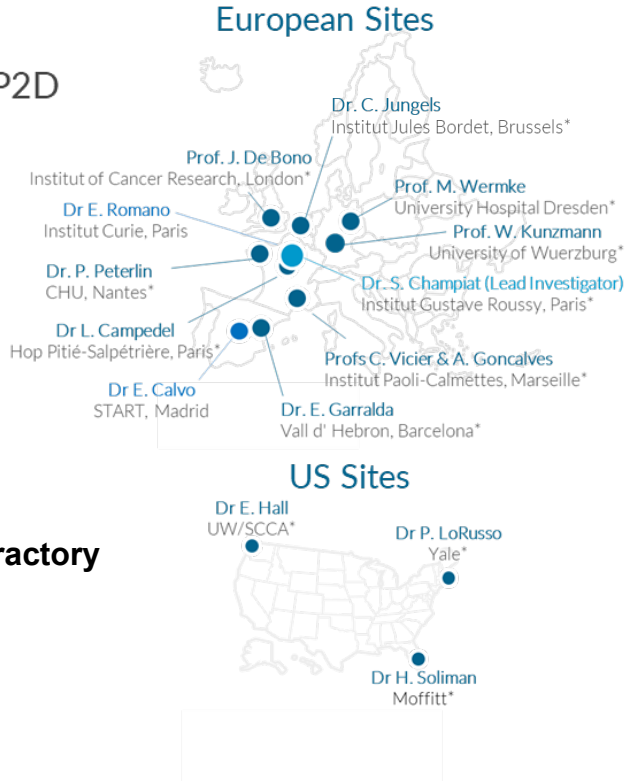
Objectives: Safety, Biomarker-derived Target Engagement & Identify RP2D

A. MonoTx Mixed Solid Tumor
Bladder, breast, colorectal, gastric, melanoma, ovarian, prostate, PDAC
Completed N = 33 (20 µg to 200 mg)

B. MonoTx Hematologic
AML, ALL, FL, DLBCL
Recruiting N = 20 (200 µg to 75 mg)

C. Pembro Combo
Bladder, HNSCC, melanoma & NSCLC
Completed N = 40 (700 µg to 200 mg)

Anti-PD(L)1 primary or secondary refractory



EVICTION: Safety of ICT01 in Combination with Pembrolizumab

Common (>10%) Related Treatment-Emergent Adverse Events (Safety Population*)

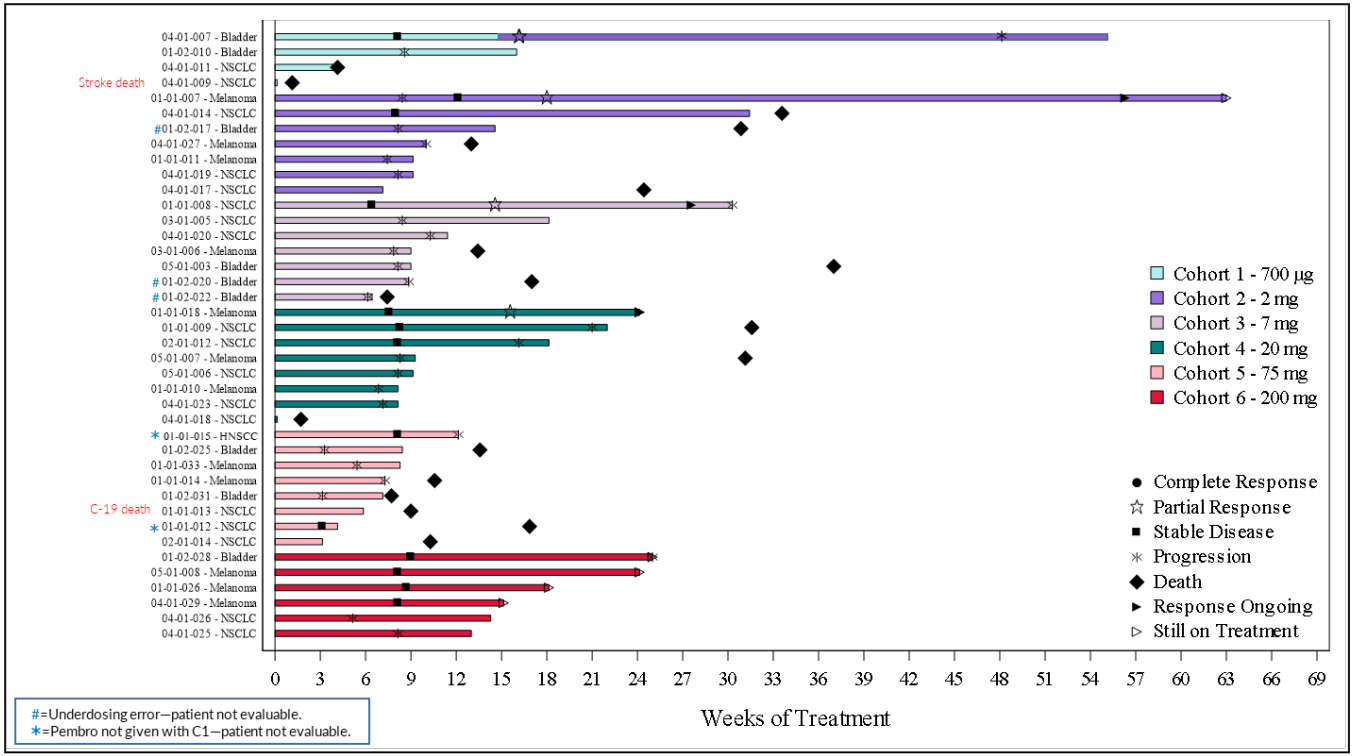
	ICT01 Dose plus 200 mg Pembrolizumab						
	700 µg (N=4) n (%) E	**2 mg** (N=8) n (%) E	**7 mg** (N=8) n (%) E	**20 mg** (N=8) n (%) E	**75 mg** (N=8) n (%) E	**200 mg** (N=6) n (%) E	**Overall** (N=40) n (%) E
Related Grade 3 or Higher	0	1 (12) 1	0	3 (38) 3	2 (25) 5	0	6 (15) 9
Preferred Term[1]							
Pyrexia	0	1 (12) 1	2 (25) 3	6 (75) 8	5 (62) 5	3 (50) 3	17 (42) 20
Asthenia	1 (25) 1	1 (12) 3	3 (38) 3	1 (12) 1	2 (25) 5	1 (17) 2	9 (22) 15
Chills	0	1 (12) 1	3 (38) 4	2 (25) 4	2 (25) 2	1 (17) 1	9 (22) 12
Cytokine release syndrome	0	1 (12) 1	2 (25) 2	1 (12) 3	2 (25) 2	2 (33) 2	8 (20) 10
Hypoxia	0	0	2 (12) 2	2 (25) 2	0	1 (17) 1	5 (12) 5
Alanine aminotransferase increased	1 (25) 1	0	1 (12) 1	0	1 (12) 1	1 (17) 1	4 (10) 4
Aspartate aminotransferase increased	1 (25) 1	0	1 (12) 1	1 (12) 1	0	1 (17) 1	4 (10) 4
Decreased appetite	1 (25) 1	0	0	1 (12) 1	2 (25) 2	0	4 (10) 4

* Patients must have received at least 1 dose of ICT01; n = number of unique patients experiencing an event; E = total number of events; CRS comprises fever, chills ± hypotension ± tachycardia
[1] Adverse events are coded to preferred term using MedDRA, version 23.1.

ICT01 Safety Summary:

1. No DLTs have been observed to date with ICT01 with pembrolizumab (or as monotherapy)
2. No Grade 4 or 5 TEAEs related to ICT01.
3. Similar AE profile for monotherapy in solid and hematologic cancers, and in combo with pembro

Swimmer Plot of Solid Tumor Patients (n=40) who Failed ≥1 Prior CPI Receiving ICT01 plus Pembrolizumab

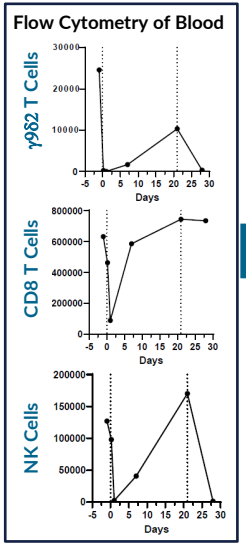


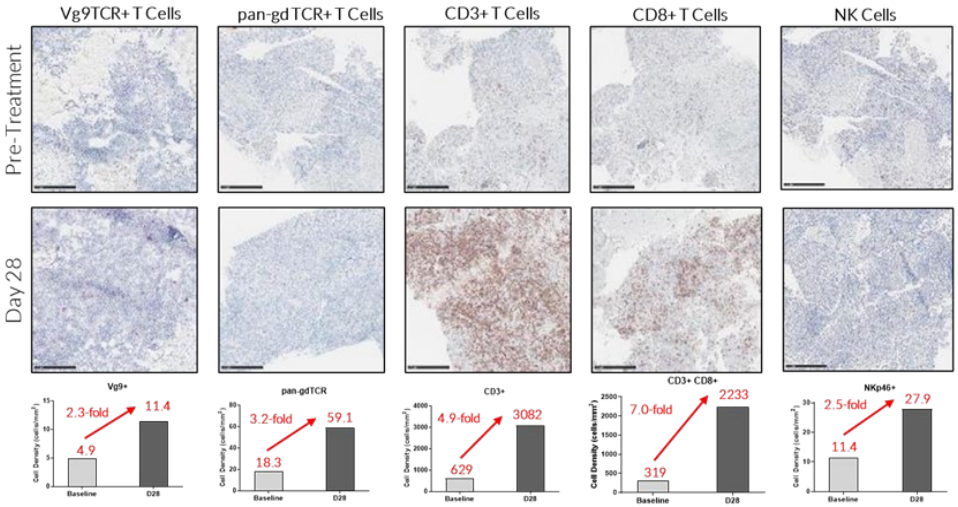
Disease Control Rate (≥ SD) by Indication:

Melanoma: 5/12 (42%)
NSCLC: 4/18 (22%)
Bladder: 2/9 (22%)
HNSCC: 1/1

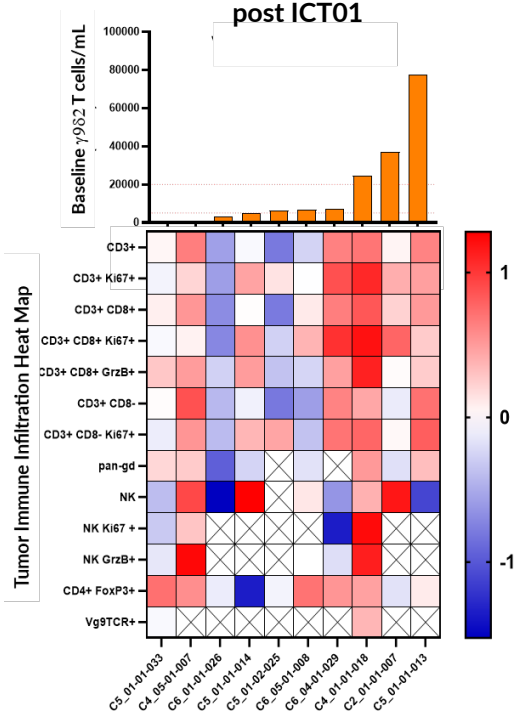
ICT01 + Pembro Remodels the TME in Patients with Ipi/Nivo-Refractory Melanoma: Relationship with γ9δ2 T Cell Counts

53yo F Dx: 2019 20 mg ICT01 + Pembro Start: 4-Jan-2022	**Prior Therapy** IPI / NIVO 6/21-10/21	**Baseline γ9δ2 T cells** 24611	**Baseline Target Lesions:** 104mm (n=1)	**PR W16/24** -42%





Group C: Higher Baseline γ9δ2 T Cells Improve Tumor Infiltration post ICT01



Peripheral activation/migration leads to enhanced tumor infiltration of γδ, CD3, CD8 and NK cells in every type of solid tumor evaluated with patient's baseline γ9δ2 T cell count >5K generally associated with enhanced infiltration and probability of clinical benefit.

Conclusion: ICT01 + Pembrolizumab Combination in EVICTION

1. **ICT01 in combination with Pembrolizumab has a favorable safety profile**
   - No DLTs observed, no grade 4-5
   - No additive toxicity compared to monotherapy

2. **Encouraging activity signals observed in anti-PD(L)1 refractory patients with melanoma, NSCLC, and bladder cancer across a range of ICT01 doses**

3. **Translational data show enhanced tumor infiltration of γδ, CD3, CD8 and NK cells with better clinical outcomes dependent on patient's baseline γ9δ2 T cell counts**

4. **Phase IIa Expansion cohorts planned in melanoma, bladder cancer, and HNSCC**
   - Patient Enrichment Strategy: Screening γ9δ2 T peripheral cell count **>5000/mm^3** to be eligible

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