2022 ASCO® ANNUAL MEETING

INTERIM SAFETY AND EFFICACY RESULTS FROM AURELIO-03

A phase 1 dose escalation study of the IL-2/IL-15R βγ Receptor superagonist SOT101 as a single agent and in combination with pembrolizumab in patients with advanced solid tumors

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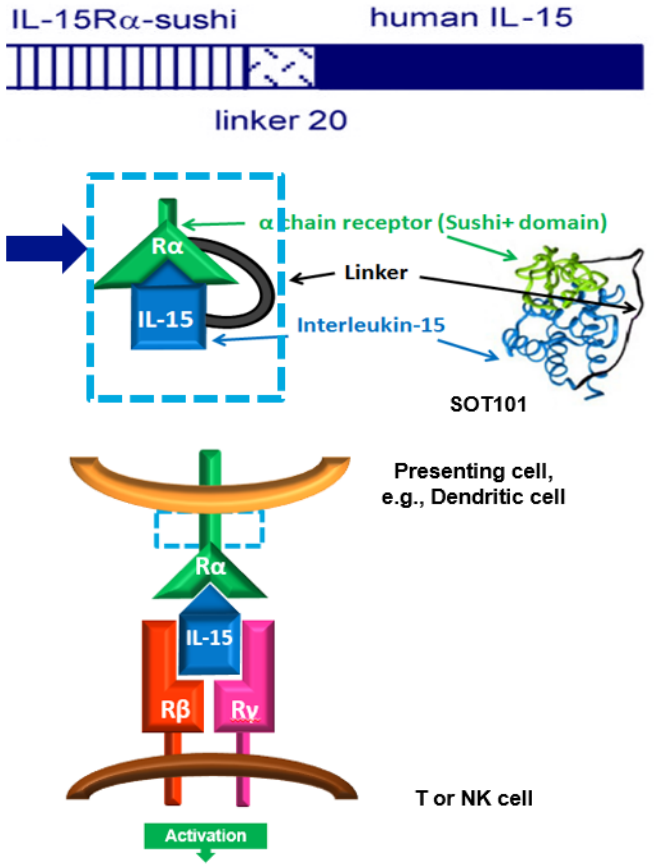
INTRODUCTION

- SOT101 is a fusion protein containing IL-15 and the Sushi+ domain of IL-15Rα[1]
- SOT101 mimics the high-affinity binding of IL-15 trans-presented to its βγ receptor at the synapse[1]
- SOT101 has shown potent anti-tumor efficacy and induction of protective memory response in mouse tumor models[2,3]
- SOT101 and programmed cell death protein 1 antibodies had synergistic effects in mouse tumor models[2]
- SOT101 may have better efficacy than other IL2/IL-15 compounds because of a strong and well-balanced induction of both innate and adaptive immunity



1. Mortier E, et al. J Biol Chem 2006; 281(3):1612-1619; 2. Desbois M, et al. J Immunol 2016;197(1):168-178; 3. Bessard A, et al. Mol Cancer Ther. 2009 Sep;8(9):2736-45
SOT101, previously SO-C101, RLI-15; IL-15, Interleukin-15; IL-15Rα, Interleukin-15 Receptor alpha; IL-2, Interleukin-2

AURELIO-03 STUDY OVERVIEW

Key Eligibility

- Advanced/metastatic solid tumors
- ECOG PS 0-1
- Measurable disease per iRECIST
- Adequate organ function
- No prior treatment with IL-2 or IL-15 like agonists
- Prior CPI allowed

- SOT101, s.c., on days 1, 2, 8, 9
- Pembrolizumab 200 mg i.v.

every 3 weeks until disease progression or unacceptable toxicity

Treatment

Part A
SOT101 monotherapy

15.0 µg/kg ((n=4)
12.0 µg/kg (n=6)
9.0 µg/kg (n=4)
6.0 µg/kg (n=3)
3.0 µg/kg (n=4)
1.5 µg/kg (n=3)
0.75 µg/kg (n=3)
0.25 µg/kg (n=3)

cross-over to combination allowed, if progression

Part B
SOT101 in combination with pembrolizumab

12.0 µg/kg (n=5)
9.0 µg/kg (n=3)
6.0 µg/kg (n=7)
3.0 µg/kg (n=3)
1.5 µg/kg (n=3)

3+3 Dose Escalation Design

Main Objectives

Primary
- Safety and tolerability
- Determination of SOT101 RP2D

Secondary
- PK and PD of SOT101 in peripheral blood
- Preliminary efficacy
- Immunogenicity of SOT101

Exploratory
- Mechanistic effect of SOT101 on selected immune cell populations in tumor tissue samples

Clinical Trails.gov Identifier NCT04234113
ECOG PS, Eastern Cooperative Oncology Group performance status; iRECIST, Response Evaluation Criteria In Solid Tumors for immune-based therapeutics; CPI, check-point inhibitor; s.c., subcutaneously; i.v., intravenously; RP2D, recommended phase 2 dose; PK, pharmacokinetics; PD, pharmacodynamics

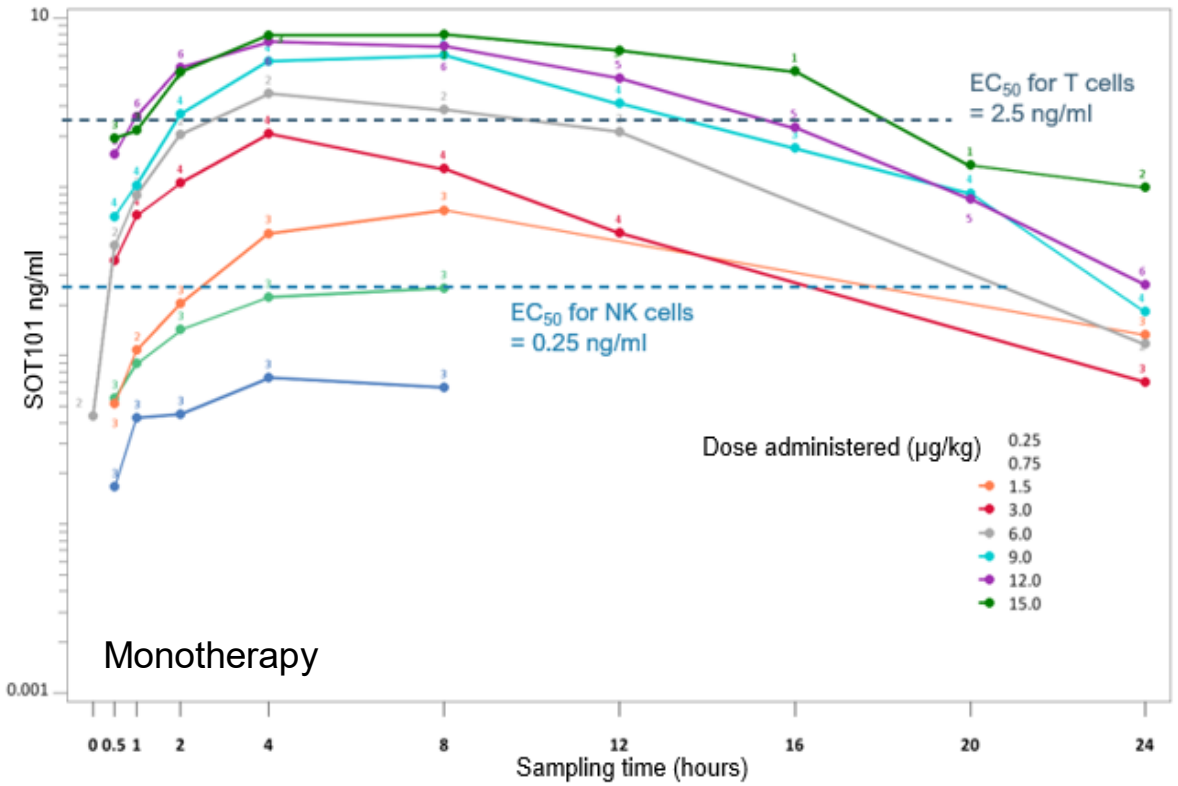
BASELINE CHARACTERISTICS

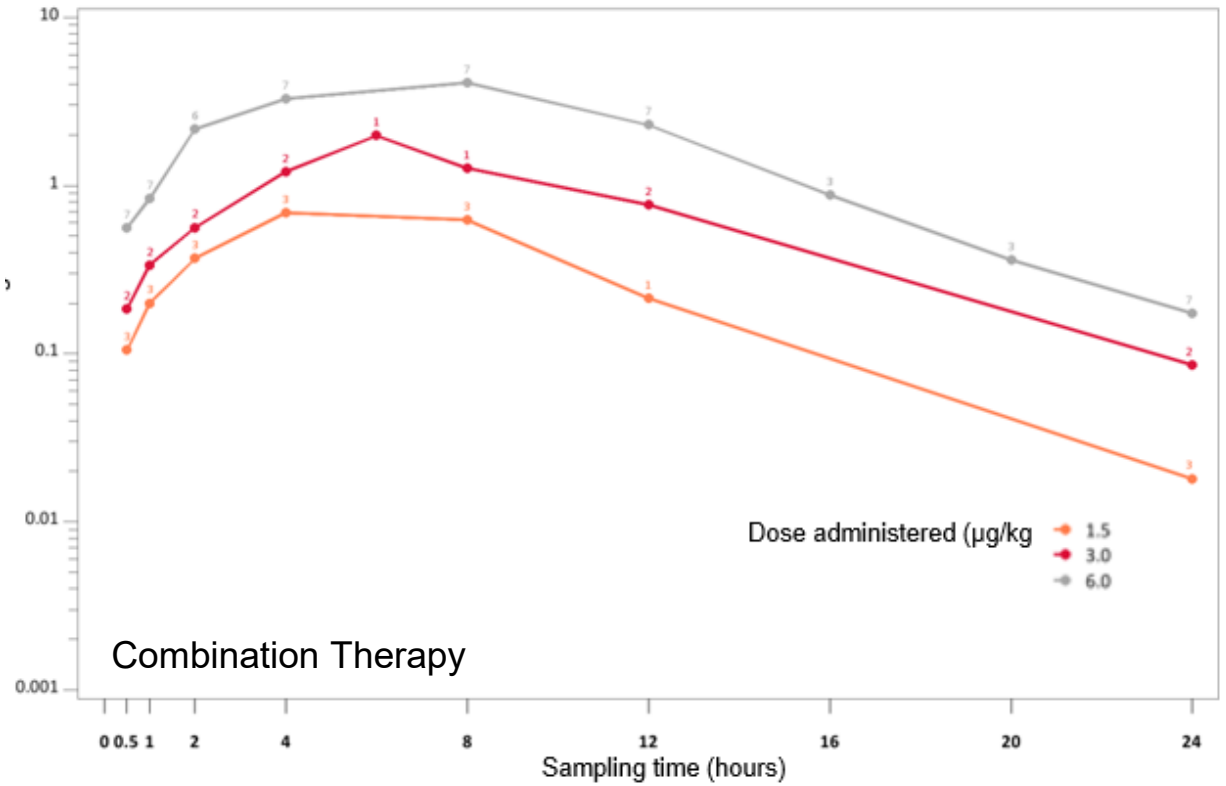
Part A: monotherapy		Part B: combination therapy
n = 30	**Patients treated**	n = 21
59 (31-80)	**Age, mean (range)**	62 (46–78)
16/14	**Gender m/f, n**	10/11
13/17	**ECOG PS 0/1, n**	14/7
	Prior systemic therapies	
3 (1-9)	No. of Lines, median (range), n	2 (1-6)
19 (63.3%)	≥ 3 Lines, n (%)	10 (47.6%)
19 (63.3%)	Prior CPI, n (%)	12 (57.1%)
9 (30.0%), 5 (16.7%), 5 (16.7%)	CPI refractory, relapsed, unknown; n (%)	2 (9.5%), 9 (42.9%), 1 (4.8%)
Biliary tract adeno (4), Merkel cell (3), Renal clear cell (2), Bladder urothelial (2), NSCLC (2), SSCC (2), Tonsil SCC (2), Ovarian clear cell, Gastro-esophageal adeno, Skin melanoma, Cervix adeno, Anal epidermoid, SSCC, Renal papillar, Ovarian mucinous, Bladder papillar, Thymus, Thyroid follicular, Ocular internal canthus SCC	**Tumor entities (n, if >1)**	CRC (3, MSI-H 2), Melanoma (3), Gastric Cancer (2), Anal SCC (2), Mesothelioma (2), Ampullary adeno, Ovarian sarcoma, Thyroid medullary, SSCC, Cervix adeno, Bladder urothelial, Liver cholangio, Cervix squamous, Biliary tract adeno

In both Part A and Part B, the majority of patients had received previous CPI treatment

NSCLC, non-small cell lung cancer; SSCC, skin squamous cell carcinoma; SCC, squamous cell carcinoma; m, male; f, female; CRC, colorectal cancer; MSI-H, microsatellite instability-high

PK: SOT101 PLASMA CONCENTRATION





Approximately dose proportional increase of exposure

Time to maximum plasma concentration approx. 5-6 hours after administration. Terminal half-life in 4 hours range

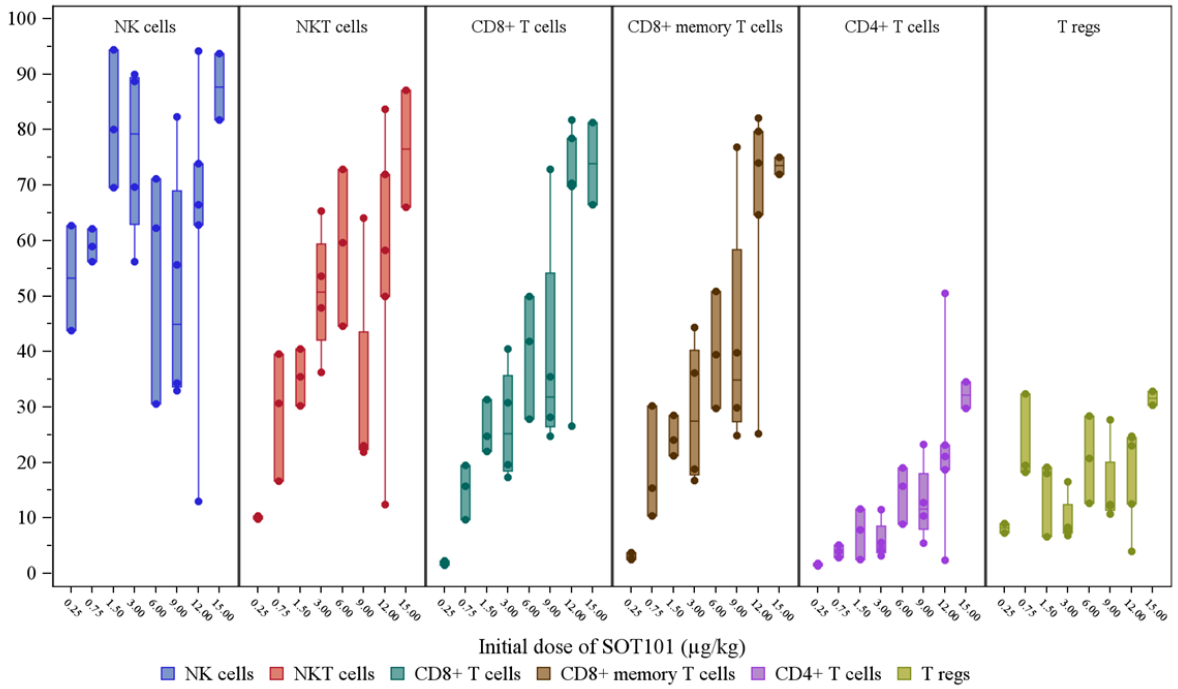
Similar SOT101 PK profile for both mono- and combination therapy with pembrolizumab

EC_{50}; half maximal effective concentration

PHARMACODYNAMICS

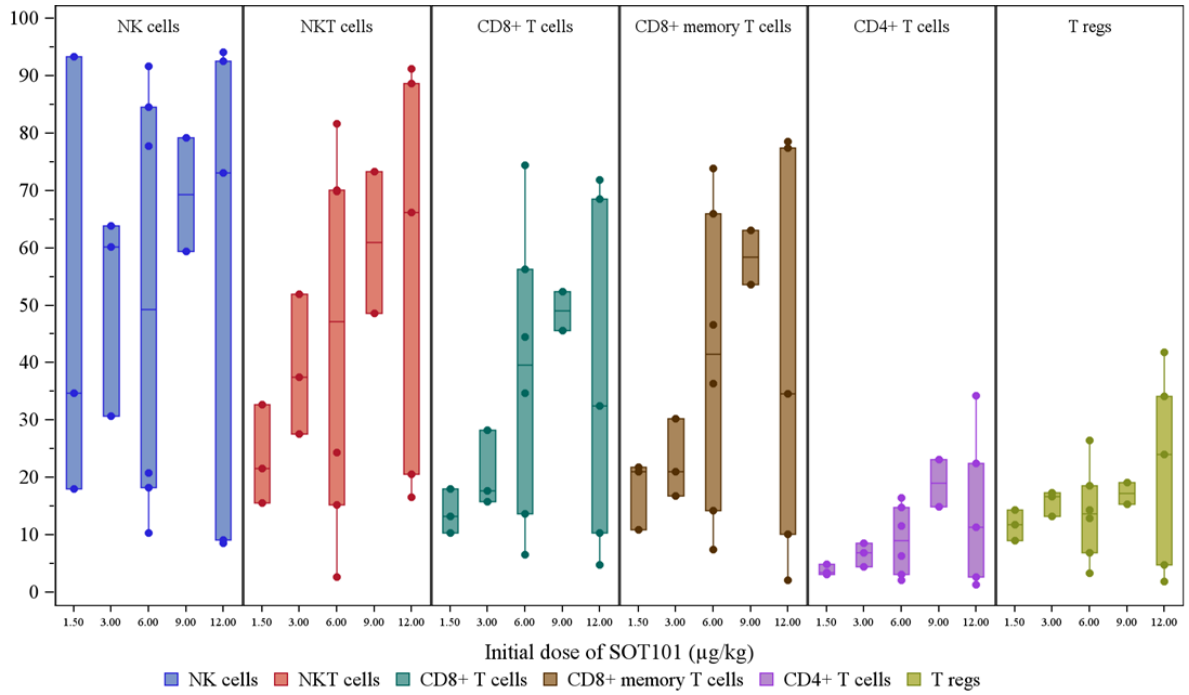
Immune cell proliferation monotherapy

Cycle 1 Day 6



Immune cell proliferation combination therapy

Cycle 1 Day 6



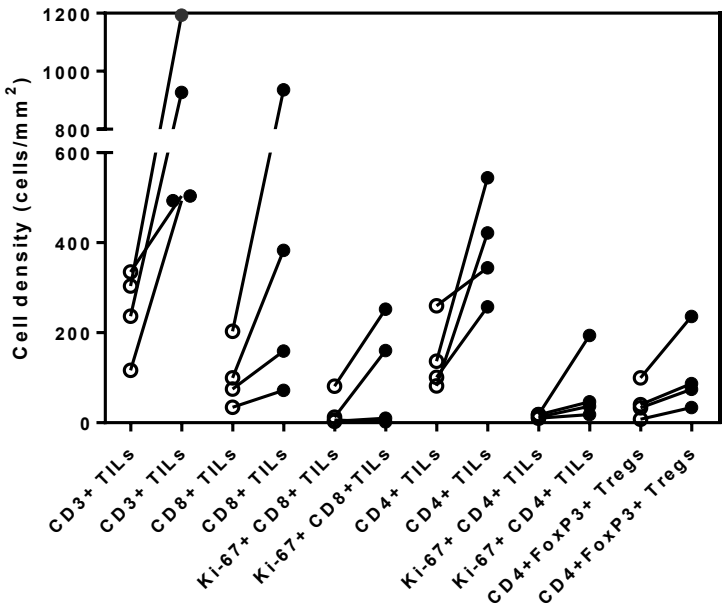
SOT101 promotes proliferation of target immune cells without T regulatory cell activation in line with expected mode-of-action

Maximum NK cell activation already reached at low dose levels

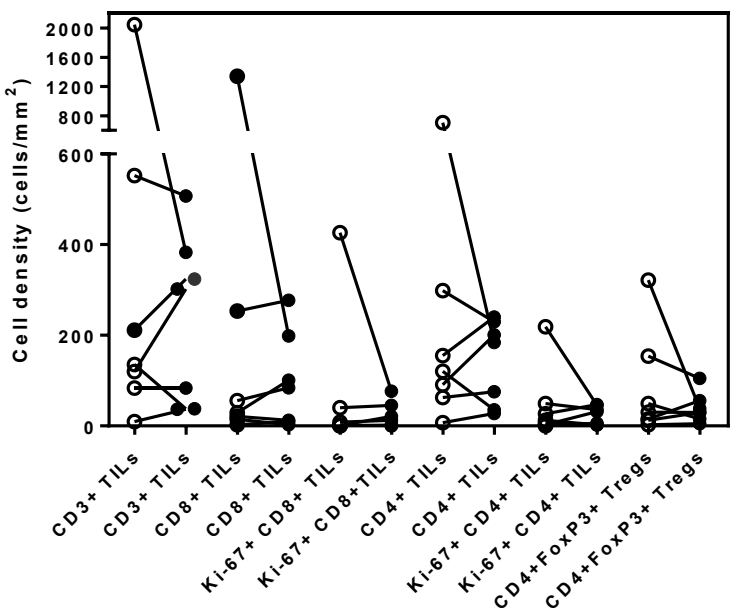
Maximum CD8⁺ T cell activation from 9 to 12 µg/kg

TUMOR IMMUNE CELL DENSITY – MONOTHERAPY

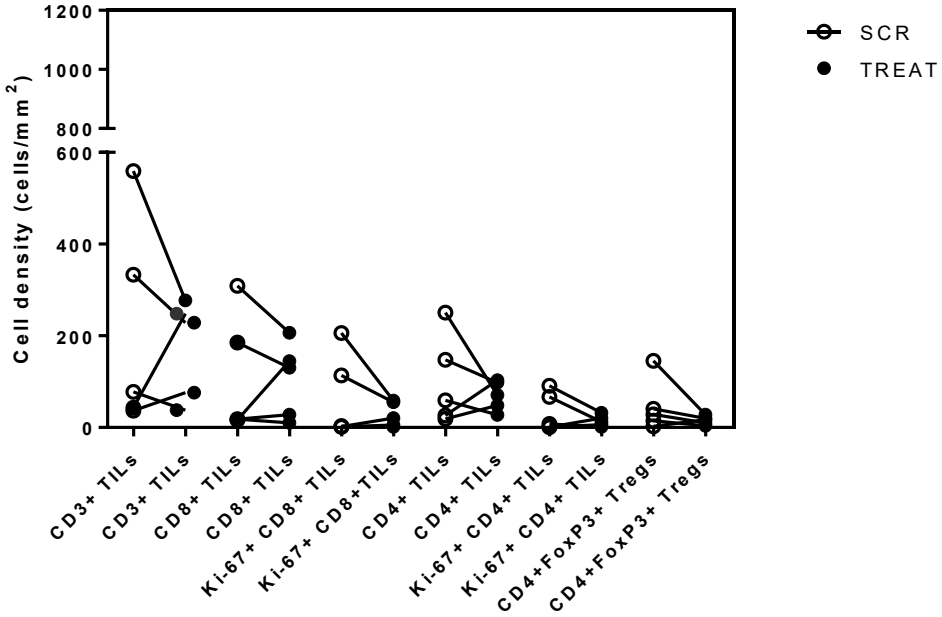
Patients with PR or ≥2xSD



Patients with 1xSD



Patients with PD

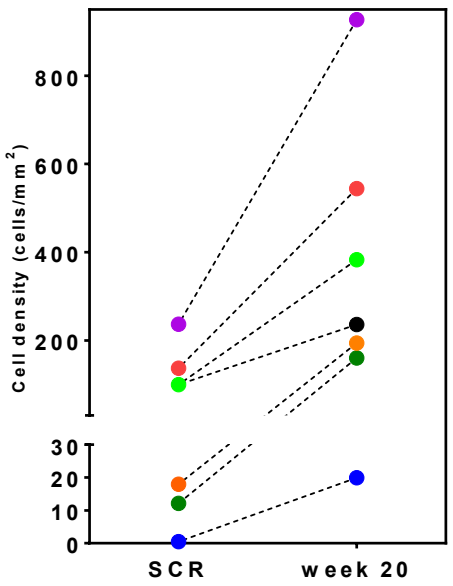


All patients with best clinical response (PR or ≥2SD) show increased TILs density in tumors after treatment

PD, progressive disease; PR, partial response; SCR, screening; SD, stable disease; TIL, tumor-infiltrating lymphocyte; TREAT, treatment

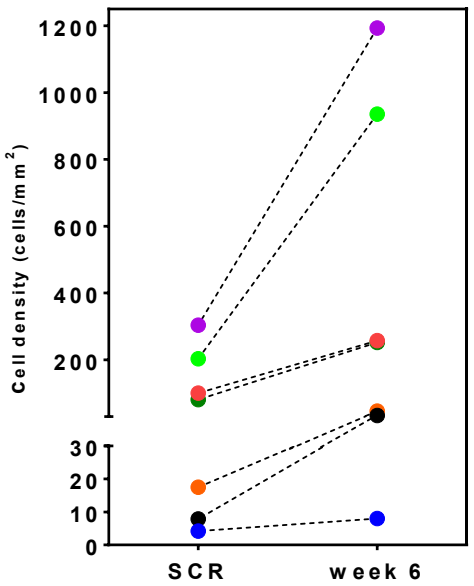
IMMUNE CELL DENSITY – MONOTHERAPY IN BEST RESPONDERS

SSCC, CPI refractory
SOT101 6.0 µg/kg



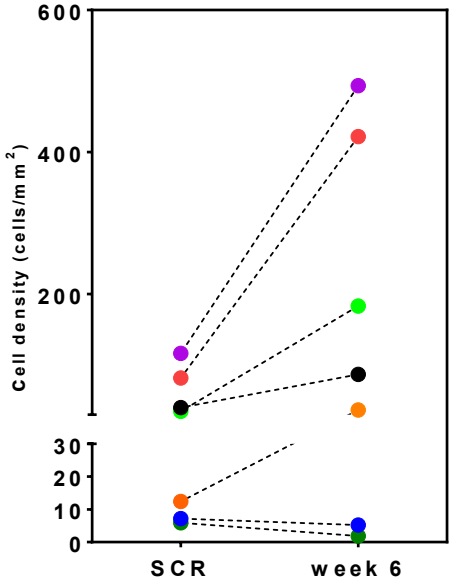
PR (-58% at cycle 8)

Kidney, CPI refractory
SOT101 6.0 µg/kg



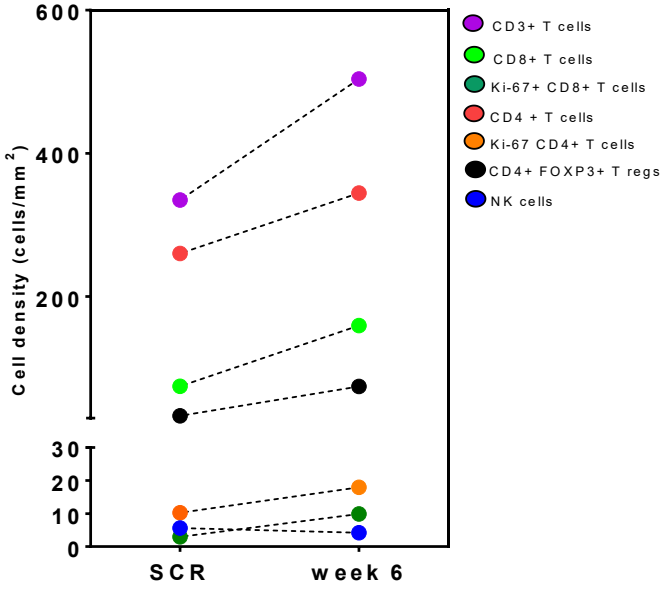
2 x SD

NSCLC
SOT101 9.0 µg/kg



2 x SD

Biliary tract
SOT101 12.0 µg/kg

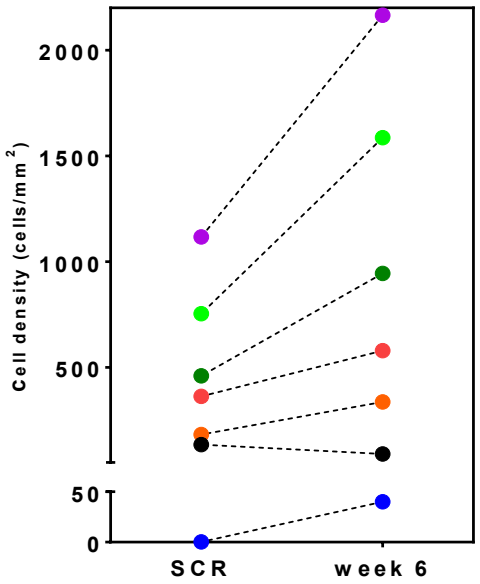


2 x SD

Increased immune cell density in tumor tissue from patients with PR or confirmed SD

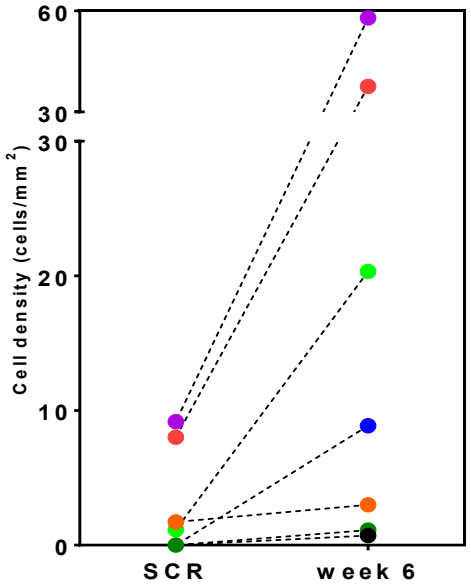
IMMUNE CELL DENSITY – COMBINATION THERAPY

Anal SCC, CPI refractory, SOT101 1.5 µg/kg



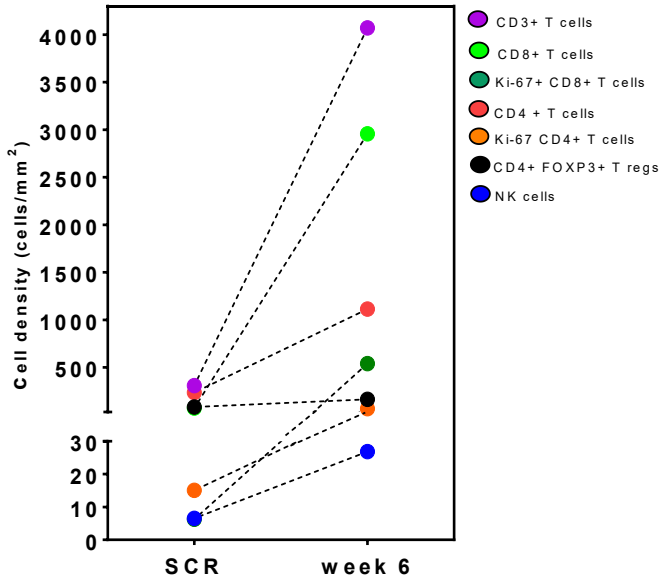
7 x SD

Thyroid gland SOT101 3.0 µg/kg



PR (-36% after 10 cycles)

Cervix uteri SOT101 6.0 µg/kg

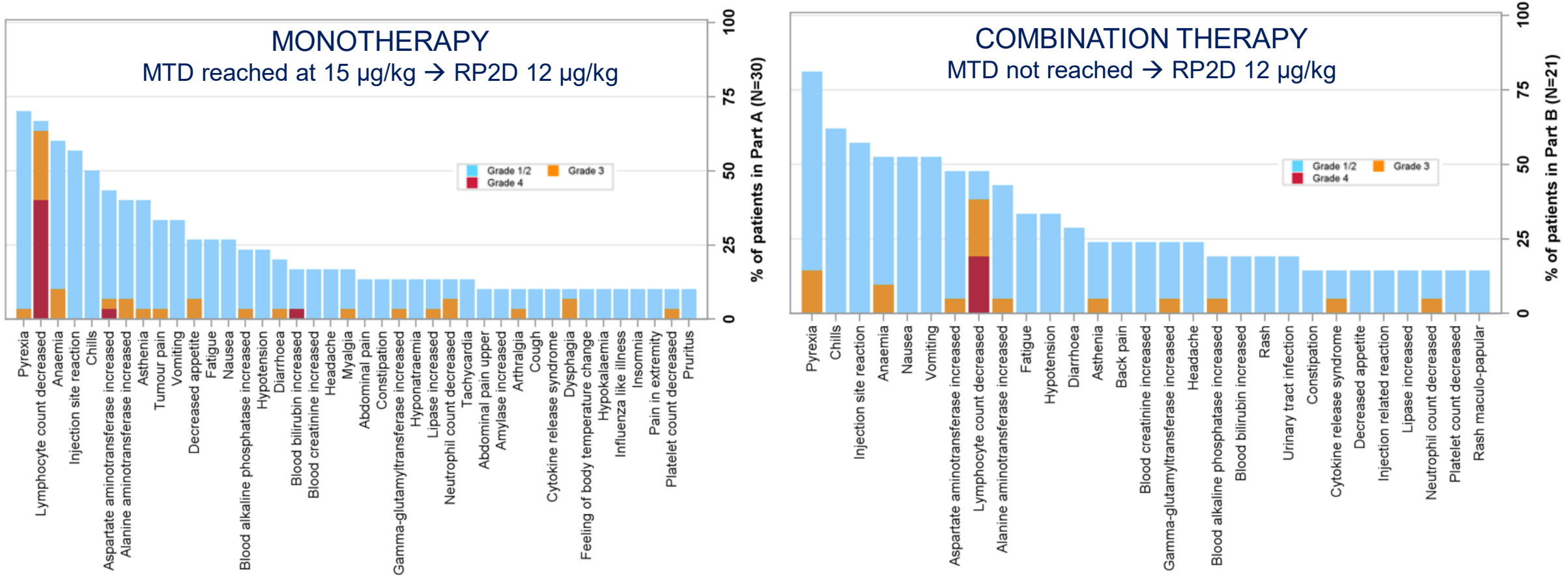


4 x SD

Increased immune cell density in tumor tissue from patients with PR or confirmed SD

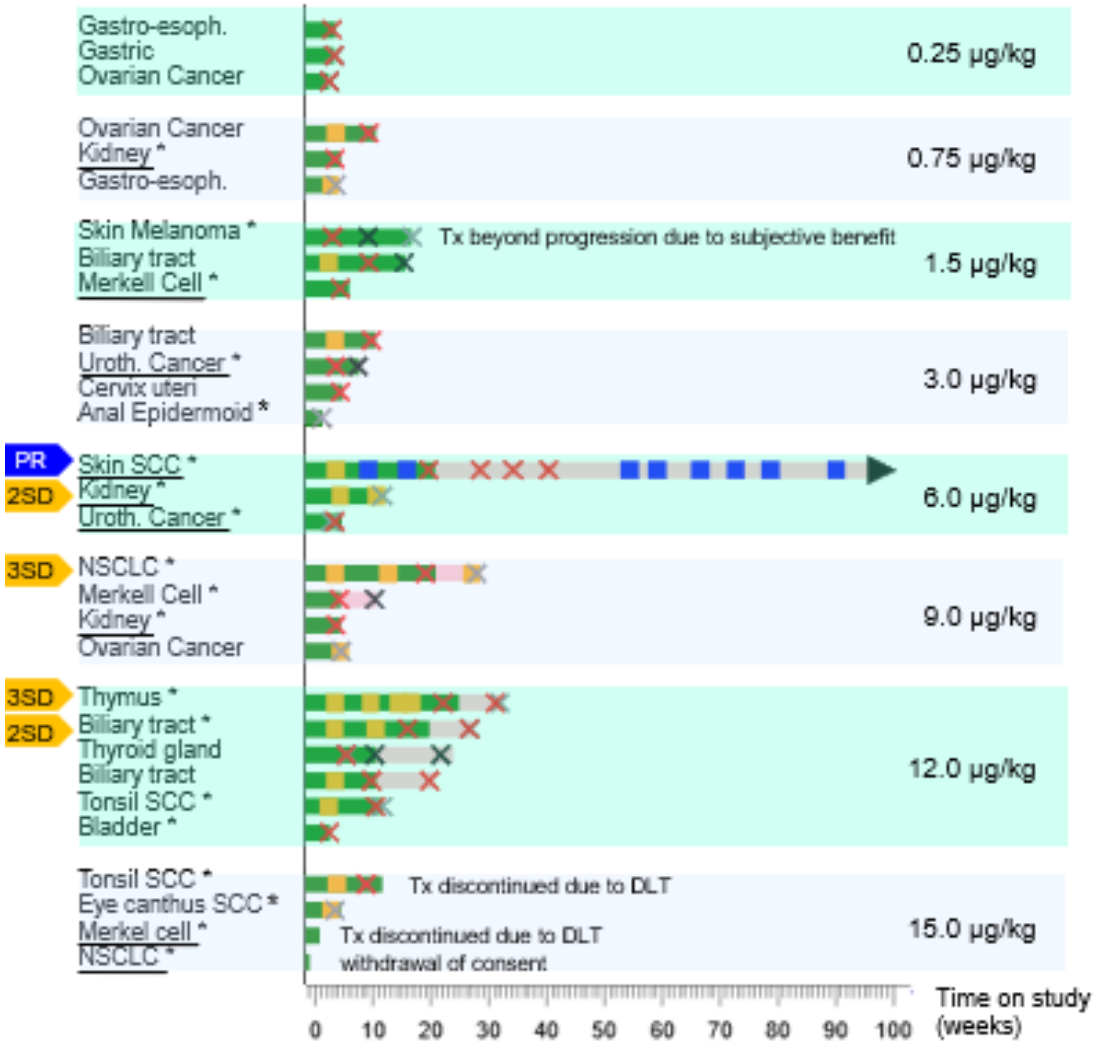
SAFETY AND RECOMMENDED PHASE 2 DOSE

PERCENTAGE OF TEAES IN ≥ 10% OF PATIENTS AND MAXIMUM SEVERITY ACROSS ALL DOSE LEVELS



AE profile combination therapy in line with AE profile of either compound in monotherapy → no additive toxicity
RP2D defined as SOT101 dose level 12 µg/kg

INTERIM EFFICACY – MONOTHERAPY



Tx, treatment; UPD, unconfirmed progressive disease; CPD, confirmed progressive disease

Monotherapy

- 1 confirmed Partial Response
- 11 stable disease – 4 with ≥ 2xSD

Clinical benefit* observed in 8 out of 13 patients at dose-levels 6 to 12 µg/kg with at least one evaluable post-BL tumor assessment

- PR
- SD
- × Clinical progression
- × UPD
- × CPD
- ▲ Treatment Ongoing

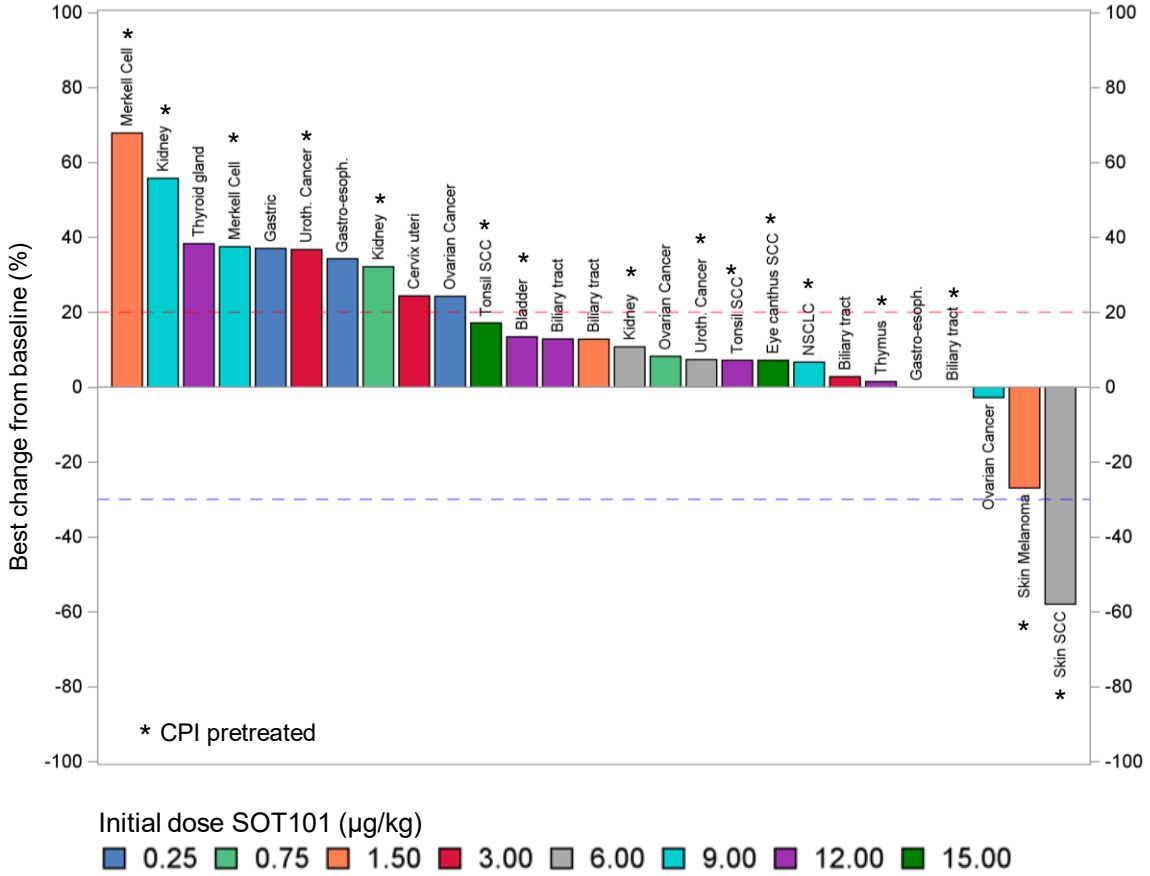
* CPI-pretreated (primary refractory)

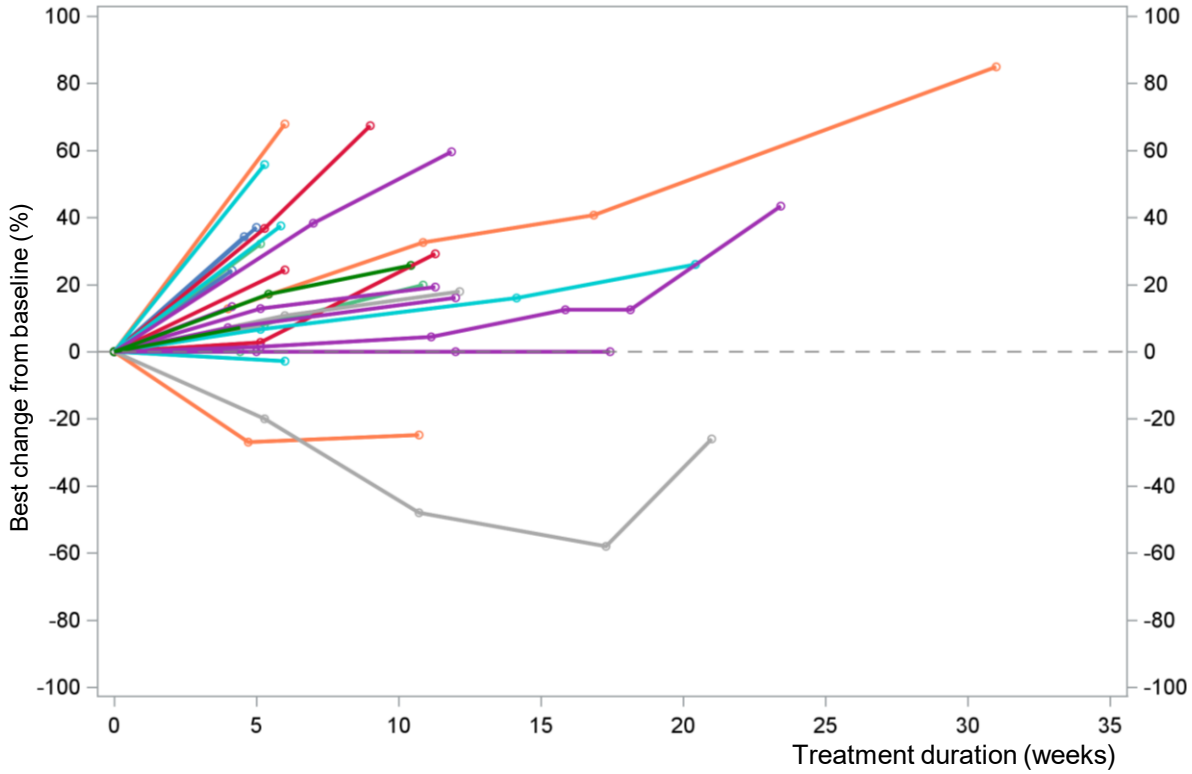
Cross-over

- 1 confirmed Partial Response, ongoing > 22 weeks

*Considered as at least 1 occurrence of stable disease or response

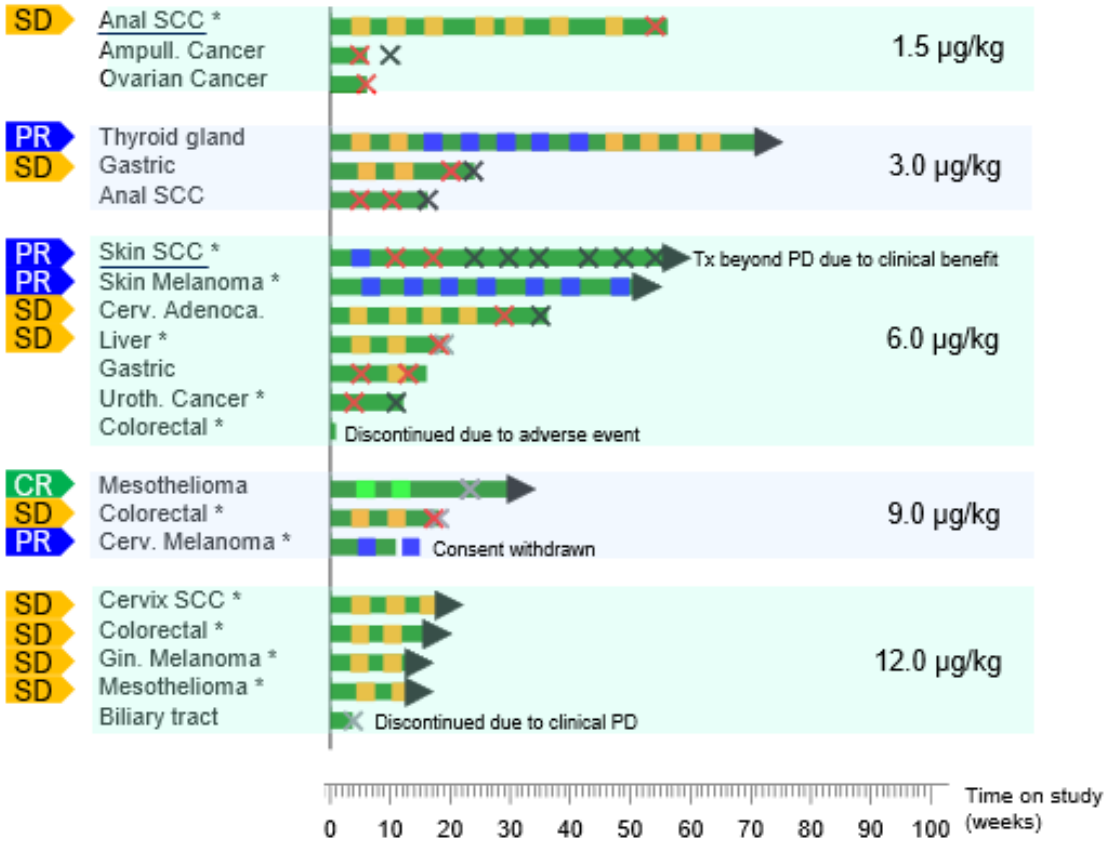
TUMOR SIZE CHANGE – MONOTHERAPY





Tumor size is displayed as the sum of target lesion diameters
Tumor data evaluated in all patients with at least one post-baseline tumor assessment

INTERIM EFFICACY – COMBINATION THERAPY



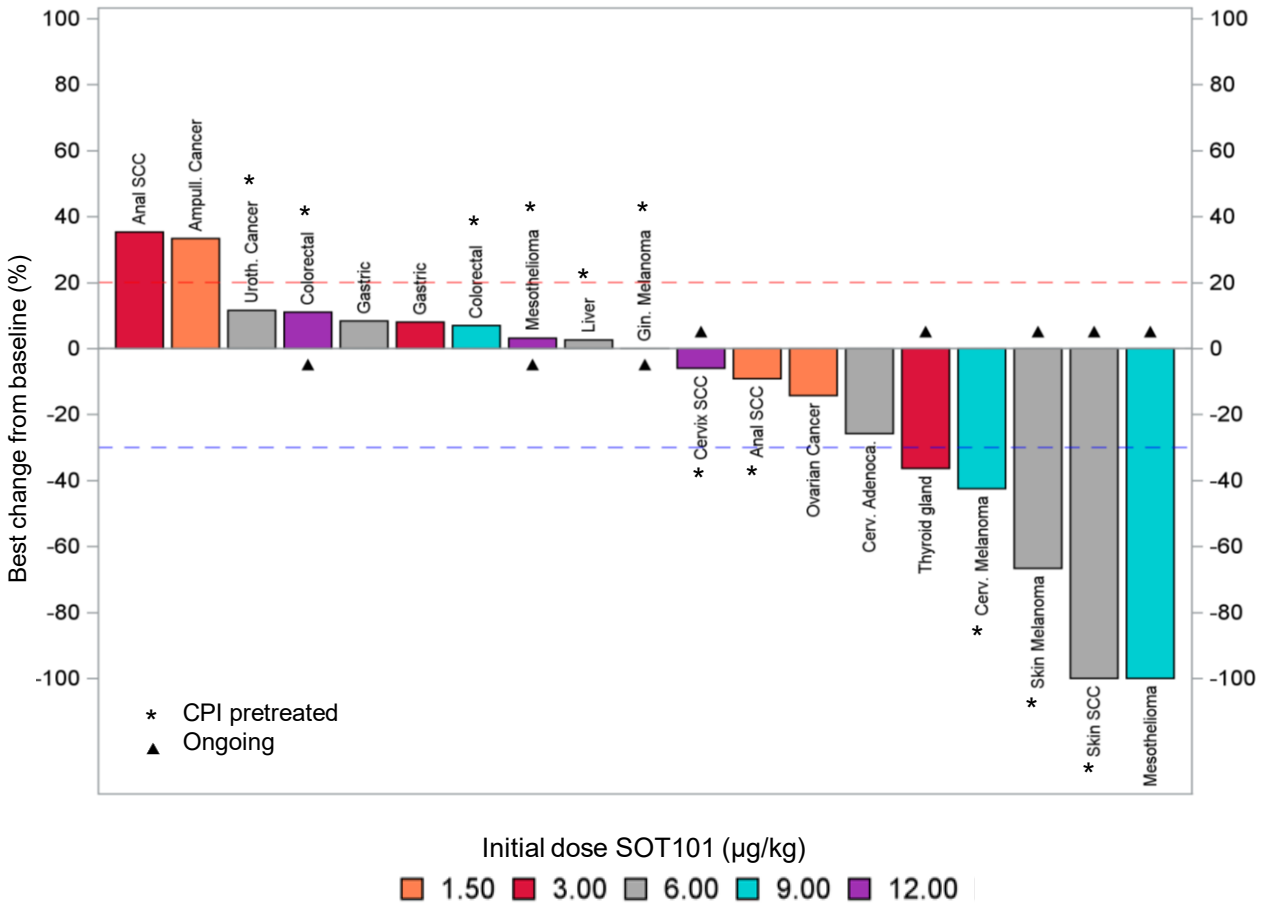
- 1 confirmed Complete Response
- 4 Partial Responses – 3 confirmed
- 10 Stable Diseases – 9 with ≥ 2xSD

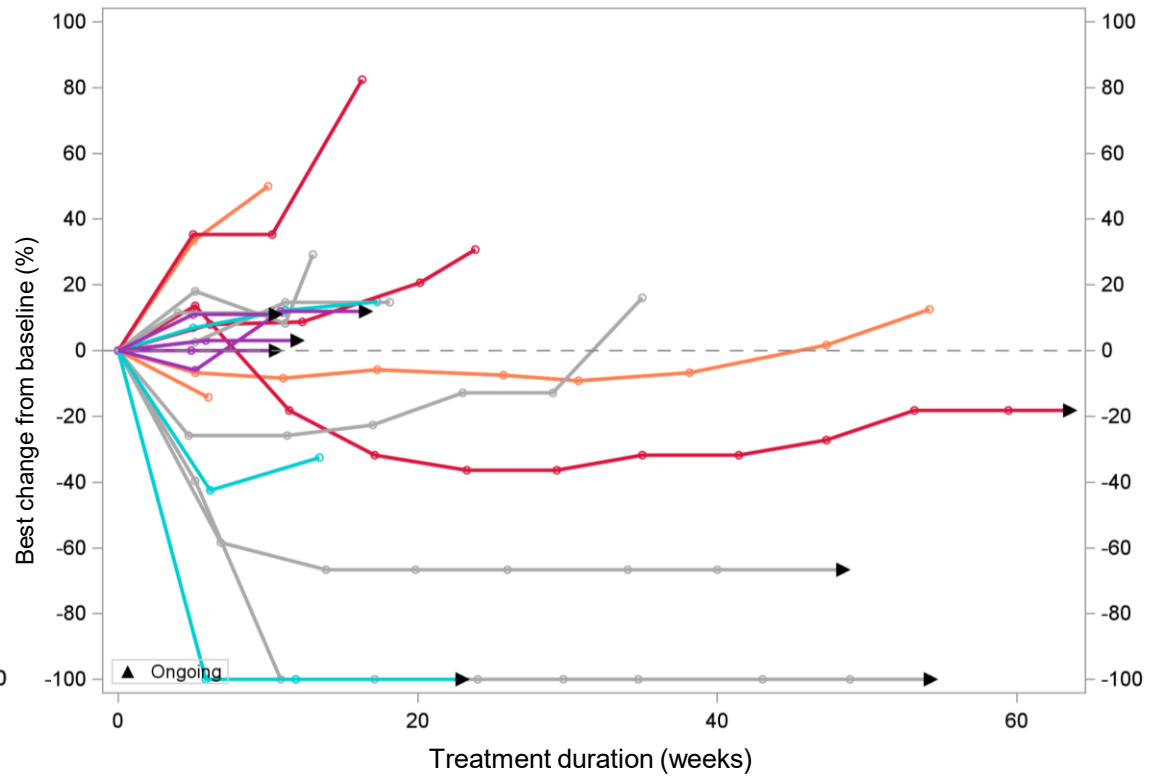
■ PR	× UPD
■ CR	× CPD
■ SD	▲ Treatment Ongoing
× Clinical progression	* CPI-pretreated (refractory)

Clinical benefit* observed in 15 out of 19 patients with at least one evaluable post-baseline tumor assessment

*Considered as at least 1 occurrence of stable disease or response

TUMOR SIZE CHANGE – COMBINATION THERAPY





Tumor size is displayed as the sum of target lesion diameters
Tumor data evaluated in all patients with at least one post-baseline tumor assessment

CASE STUDY

PARTIAL RESPONSE IN A 57 YRS MALE WITH METASTATIC MELANOMA

Initial diagnosis: Jan 2018

- Metastatic melanoma of the skin (BRAF V600+)

Previous therapies

- 2018 Surgeries: Excision of primary lesion, excision sentinel lymph nodes, bilateral neck dissection

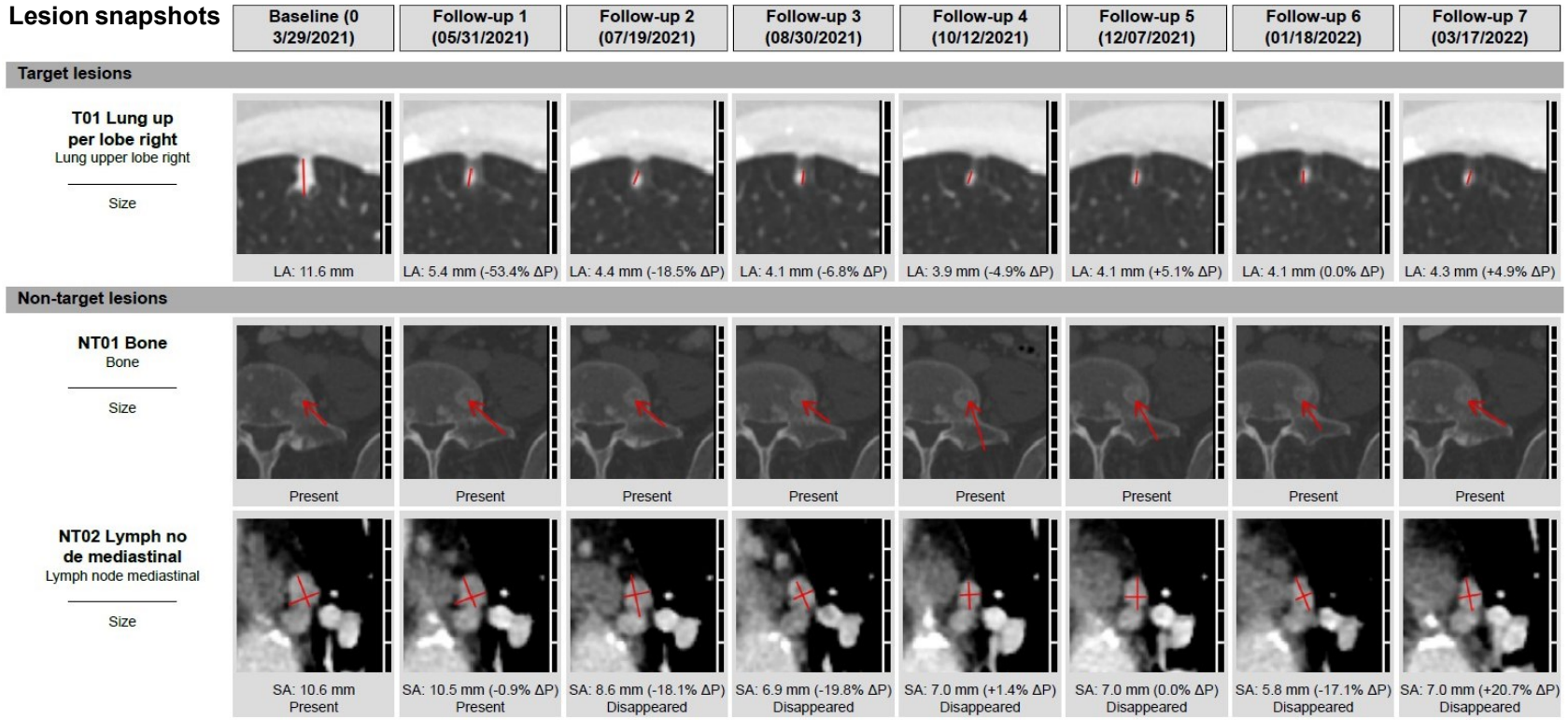
Systemic therapy

- Clinical study: anti-PDL1, dabrafenib, and trametinib
  May 2018 – Feb 2021 → relapse

Last disease progression: 23 Feb 2021

SC103 Study

- Started SOT101 6 µg/kg in combination with pembrolizumab on 14 Apr 2021
- CRS G2 after 1st dose SOT101 → reduction to SOT101 3 µg/kg for following administrations
- Ongoing with PR (TL -48.5%) in C18



Long Lasting PR in CPI-relapsed metastatic melanoma on SOT101 + pembrolizumab for more than 350 days

PDL1, programmed death ligand-1; TL, target lesion; C, cycle

CONCLUSIONS

- SOT101 monotherapy and SOT101 in combination with pembrolizumab have a favourable safety profile
  - No additive toxicity was seen when combining SOT101with pembrolizumab
- The SOT101 RP2D was defined as 12 µg/kg
- Encouraging efficacy signals were observed for monotherapy and combination therapy, even in CPI-relapsed tumors
- For monotherapy, 8 out of 13 patients had observed clinical benefit at dose-levels 6 to 12 µg/kg with at least one post-baseline tumor assessment
  - The prelimary efficacy of the RP2D is currently further evaluated in the ongoing monotherapy extension in skin squamous cell carcinoma, melanoma, and renal cell cancer
- For combination therapy, 15 out of 19 patients had observed clinical benefit with at least one post-baseline tumor assessment
  - Encouraging efficacy signals in this heavily pre-treated population will be further evaluated in AURELIO-04 (NCT05256381)

Thank you for your attention!

PRESENTED BY:
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