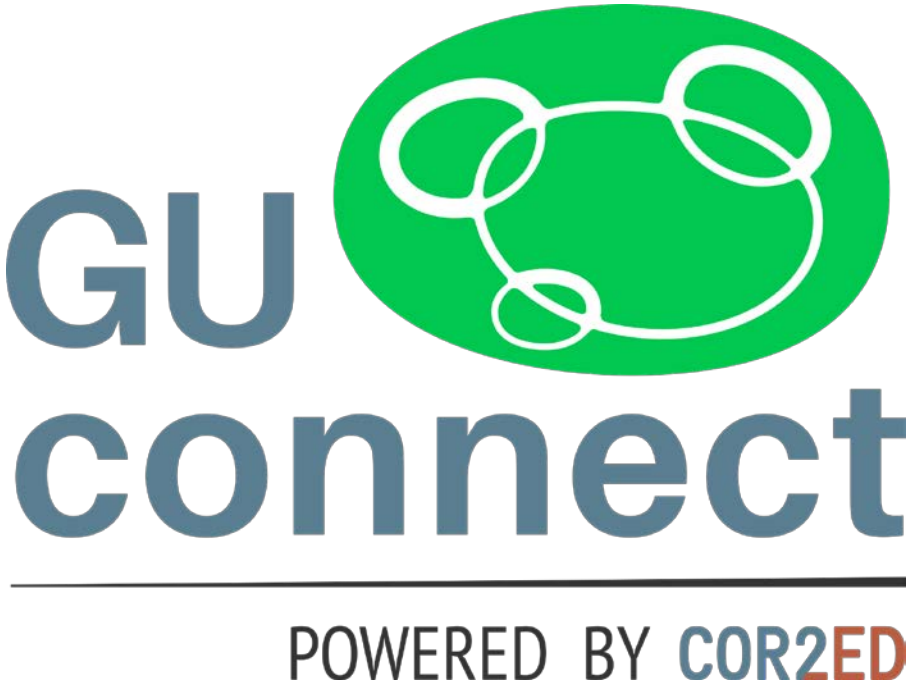
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MEETING SUMMARY
ASCO GU 2019, San Francisco, USA

Sandy Srinivas, MD
Stanford University Medical Center
California, USA

BLADDER CANCER UPDATE

DISCLAIMER

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SACITUZUMAB IN PATIENTS WITH PREVIOUSLY TREATED mUC: RESULTS FROM A PHASE I/II STUDY

Tagawa, et al. Abstract #354

mUC, metastatic urothelial cancer

BACKGROUND

- Patients with mUC who progress after platinum based chemotherapy and immune checkpoint inhibitors have poor outcomes and limited treatment options
- UC is characterized by the expression of multiple cell surface antigens suitable for specific therapeutic targeting with antibody-drug conjugates (ADCs)
- ADCs are structured from three main structural units:
  - monoclonal antibody against a specific target
  - linker molecule
  - cytotoxic agent or drug (payloads)
- Two ADCs in advanced stages of development: enfortumab and sacituzumab

ADC, Antibody drug conjugate; mUC, metastatic urothelial cancer, UC, urothelial cancer

Tagawa, S et al. ASCO GU 2019, Abstract number 354; Vlachostergios, P et al. Bladder Cancer 2018;4 (3): 247-259

ANTIBODY-DRUG CONJUGATES: UROTHELIAL CANCER

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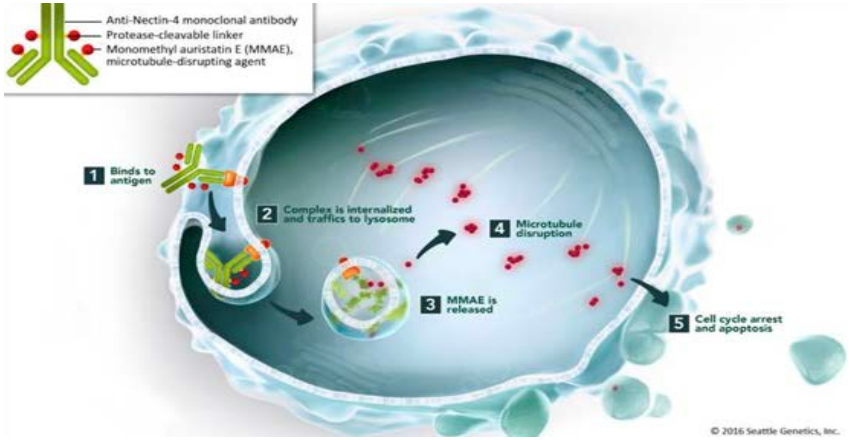
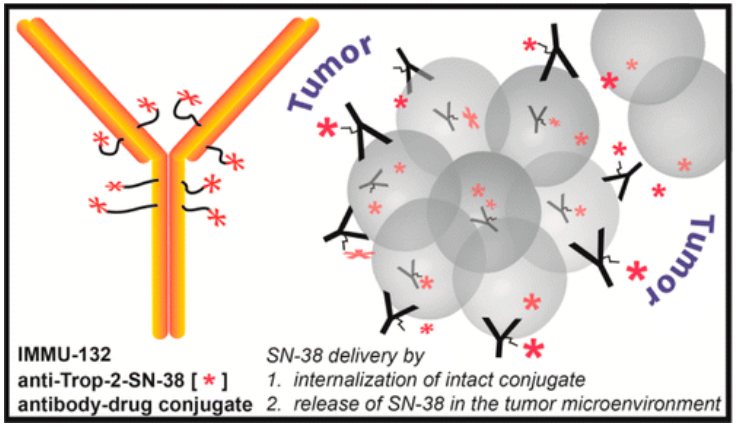
3 COMPONENTS: ANTIBODY/LINKER/PAYLOAD

Enfortumab Vedotin



Antibody- Nectin
Linker- Protease Cleavable
Payload- MMAE- microtubule

Sacituzumab Govitecan



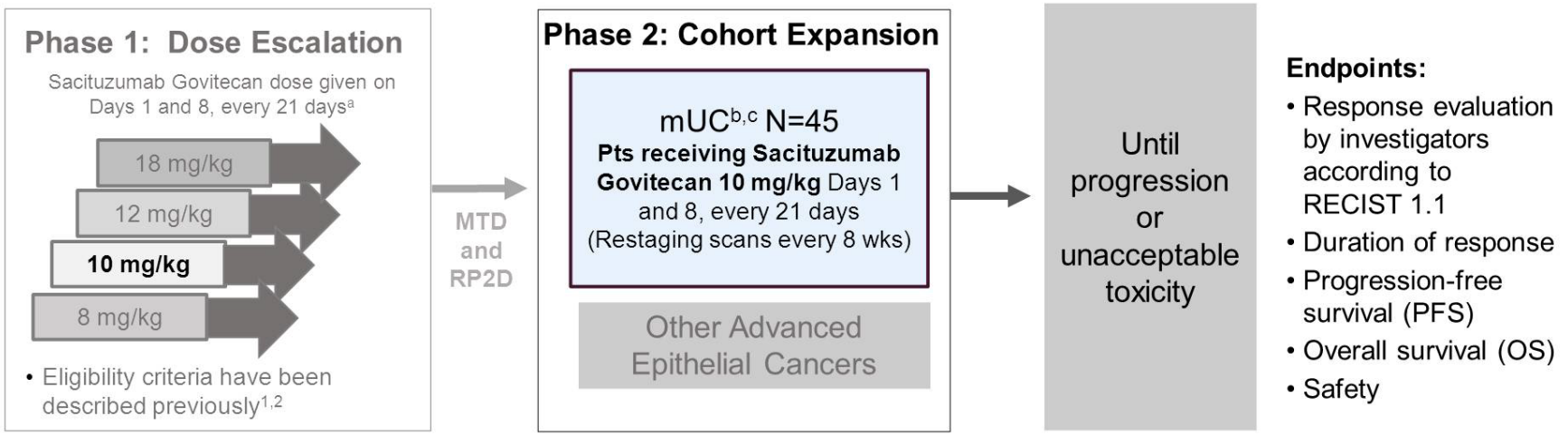
Antibody- Trop 2
Linker- Hydrolysable linker
Payload- SN-38-parent compound -Irinotecan

MMAE, monomethyl auristatin E

Rosenberg, J et al. ASCO GU 2018, Abstract number TPS542; Tagawa, S et al. ASCO GU 2019, Abstract number 354

STUDY DESIGN

SACITUZUMAB GOVITECAN – PHASE I/II, OPEN LABEL, BASKET STUDY IN PATIENTS WITH ADVANCED EPITHELIAL CANCERS



[a]All phase I pts counted in phase II population; [b]one patient in this cohort had small cell carcinoma of bladder; [c]preliminary results were reported at ESMO 2017

- mUC cohort: 45 pts on 10 mg/kg dose, 3 on 8 mg/kg dose ad 1 on 12 mg/kg dose
- Data cut off: 1st Sept 2018

MTD, maximum tolerated dose; mUC, metastatic urothelial cancer; RP2D, recommended phase 2 dose

1. Starodub A et al. Clin Cancer Res 2015, 21: 3870-8; 2. Faltas, B et al. Clin Genitourin Cancer 2016, 14:e75-79
Tagawa, S. ASCO GU 2019, Abstract number 354

RESULTS: ORR AND ADVERSE EVENTS

SACITUZUMAB GOVITECAN

	Objective Response Rate, % (n/N)	[95% CI]
Overall cohort	**31.1 (14/45)**	**[18.2, 46.6]**
Lines of prior therapies		
⩽2 prior lines	39.3 (11/28)	[21.50, 59.42]
⩾3 prior lines	17.6 (3/17)	[3.80, 43.43]
Prior checkpoint inhibitors (71% had ⩾3 prior lines of therapy)	23.5 (4/17)	[6.81, 49.90]
Prior platinum and checkpoint inhibitors	26.7 (4/15)	[7.79, 55.10]
Visceral involvement at study entry		
Yes	27.3 (9/33)	[13.30, 45.52]
Liver	33.3 (5/15)	[11.82, 61.62]
No	41.7 (5/12)	[15.17, 72.33]

Median PFS was 7.3 months and median OS was 16.3 months

Adverse Events (Worst Grade CTCAE) ⩾20% or 5% grade ⩾3 (regardless of causality; N=45)			
Event	**All grades (%)**	**Grades 3 (%)**	**Grade 4 (%)**
Diarrhea	**69**	**9**	**0**
Nausea	**67**	**2**	**0**
Fatigue	58	9	0
Neutropenia*	**51**	**22**	**16**
Constipation	44	0	0
Alopecia	40	0	0
Decreased appetite	38	0	0
Anemia	33	13	0
Cough	31	0	0
Vomiting	31	2	0
Pyrexia	24	0	0
Back pain	22	0	0
Dizziness	22	0	0
Rash	22	0	0
Hyphosphatemia	20	11	0
Febrile neutropenia	**7**	**7**	**0**

CI, confidence interval; CTCAE, common terminology criteria for adverse events; PFS, progression free survival; OS, overall survival

Tagawa, S. ASCO GU 2019, Abstract number 354

RESULTS: ENFORTUMAB VEDOTIN

- Data from a phase 1 (EV-101) study in patients with mUC demonstrated an encouraging efficacy and tolerability profile for enfortumab
- Patients were included if they had ⩾ 1 prior CT, or were cisplatin ineligible, and ECOG PS 0/1
  - Primary endpoint: AEs
  - Secondary endpoints: tumor response (CR/PR), ORR, DCR, DoR, PFS, OS
- Results were presented for 112 patients with mUC receiving the 1.25-mg/kg dose of enfortumab
- **Enfortumab** was generally **well tolerated in patients with mUC**
  - Most common all-cause grade ⩾ 3 AEs: anemia, hyponatremia, urinary tract infection, hyperglycemia
  - TRAEs (grade ⩾ 3) occurring in ⩾ 25% of patients: fatigue, decreased appetite, nausea, pruritus, diarrhea and rash
- Confirmed **ORR of ~ 40%** in heavily pretreated patients regardless of prior CPI treatment, liver metastases
- Preliminary **median OS** of **13.6 months** and **PFS** of **5.4 months**

AEs, adverse events; CPI, checkpoint inhibitor; CR, complete response; CT, chemotherapy; DCR, disease control rate; DoR, duration of response; ECOG, Eastern cooperative oncology group; mUC, metastatic urothelial cancer; ORR, objective response rate; OS, overall survival; PFS, progression free survival; PR, partial response; TRAEs, treatment related adverse events

Rosenberg, J et al. Journal of Clinical Oncology, 36 (15_suppl): 4504

CONCLUSIONS

- Antibody Drug Conjugates are a **new class of drugs**
- Effective in delivering drug to the cancer cell
- Enfortumab Vedotin and Sacituzimab Govitecan are promising drugs with **activity in heavily pretreated patients** with urothelial cancer with overall response rates of 30-40%
- Would be effective in 3rd-line Urothelial cancer when approved
- Toxicity similar to the parent compound

Rosenberg, J et al. ASCO GU 2018, Abstract number TPS542; Tagawa, S et al. ASCO GU 2019, Abstract number 354

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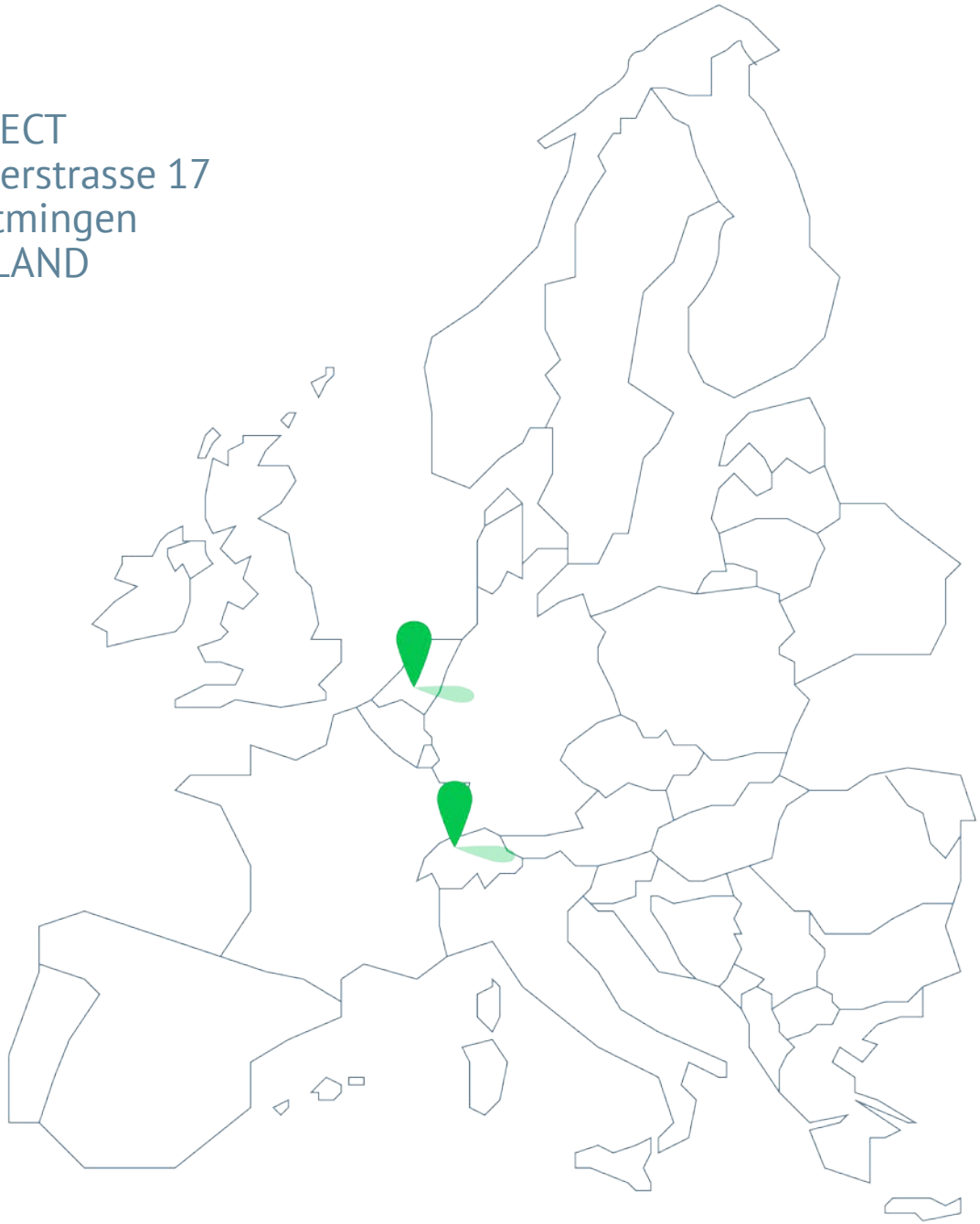

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