Safety & efficacy of adoptive cell transfer using autologous tumor infiltrating lymphocytes (LN-145) for treatment of recurrent, metastatic, or persistent cervical carcinoma

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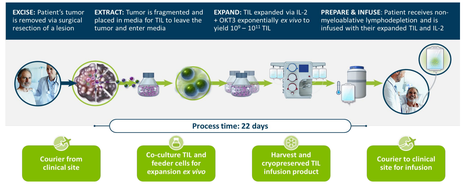
BACKGROUND

- There is a high unmet medical need for effective treatments for patients with recurrent, metastatic, or persistent cervical cancer
- Cervical cancer is a leading cause of cancer-related death in women with over 12,000 new cases and 4,000 deaths in the US alone[1]
- Most patients are young & survival rates are poor
- Objective Response Rates (ORR) for second-line therapies are between 4 and 14% for chemotherapy and recently approved immunotherapy[2]
  - Advanced recurrent, metastatic, and persistent forms of cervical cancer have poor outcomes with mean progression-free survival (PFS) rates less than 8 months following standard platinum-based chemotherapy with post-progression overall survival of 8.4 months when bevacizumab is added[3]
- Adoptive cell transfer using tumor infiltrating lymphocytes (TIL) has demonstrated durable responses in some patients with recurrent cervical cancer thus offering the potential for long-term disease control:
  - The presence of TIL has been well documented in patients with human papillomavirus (HPV)-associated cancers, including cervical carcinoma, and have been positively correlated with improved patient outcomes[4]
  - Several early studies have demonstrated the feasibility of isolation and culture of TIL from cervical tumors[5]
  - A pilot study of TIL therapy in 9 patients with previously treated cervical carcinoma demonstrated an ORR of 33% that included 2 durable long-term (46 and 54 mos) complete responses[6]
- innovaTIL-04 was designed to evaluate the efficacy and safety of LN-145, an autologous investigational TIL therapy for the treatment of patients with recurrent, metastatic, or persistent cervical carcinoma

[1] https://seer.cancer.gov
[2] Boussios S, Seraj E, Zarkavelis, G, Petrakis D, Kollas A, et al. 2016. *Crit. Rev in Oncl/Hematol.* 108:164-174.
[3] Minion LE, Tewari KS. Cervical cancer – state of the science: from angiogenesis blockade to checkpoint inhibition. 2018. *Gynecol Oncol.* 148:609–621.
[4] Shah W, Yan X, Jing L, Zhou Y, Chen H, and Wang Y. 2011. *Cell Mol Immunol.* 8:59-66.
[5] Sevanović S, Draper LM, Langhan MM, Campbell TE, Kwong ML, Wunderlich JR, Dudley ME, Yang JC, et al. 2015. *J Clin Oncol.* 33:1543-1550.
[6] Stevanović S, Pasetto A, Gartner JJ, Prickett TD, et al. 2017. *Science.* 356: 200-205.

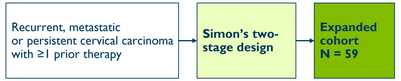
Figure 1. Cryopreserved Autologous TIL (LN-145)

Manufacturing Process: 22-Days



innovaTIL-04 Study Design

Phase 2, multicenter study to evaluate the efficacy and safety of autologous Tumor Infiltrating Lymphocytes (LN-145) in patients with recurrent, metastatic or persistent cervical carcinoma (NCT03108495)



Endpoints

- Primary: Objective Response Rate (ORR) per Response Evaluation Criteria In Solid Tumors (RECIST) v1.1
- Secondary: safety and efficacy

Key updates

- Protocol amended to increase total to 59 patients, and ORR as determined by Blinded Independent Review Committee (BIRC)
- Fast Track and Breakthrough designations received

METHODS

- Data extract as of 14 May 2019
- Safety & Efficacy Sets: 27 patients who underwent resection for the purpose of TIL generation and received LN-145 infusion

RESULTS

Table 1. Patient Characteristics

CHARACTERISTIC	N=27, (%)
Age	
Median	45
Min, Max	30, 68
Prior therapies, n (%)	
Mean # prior therapies	2.4
Platinum-Based	27 (100)
Taxane	26 (96)
Anti-VEGF	22 (82)
Radiotherapy	20 (74)
Anti-PD-1/PD-L-1	4 (15)
Cancer Status at Screening	
Metastatic	14 (52)
Recurrent	10 (37)
Persistent	3 (11)

CHARACTERISTIC	Screening	Baseline
ECOG score, n (%)		
0	19 (70)	9 (33)
1	8 (30)	17 (63)
≥2	0	1 (4)
Histologic Cell Type, n (%)		
Squamous Cell Carcinoma		12 (44)
Adenocarcinoma		12 (44)
Adenosquamous Carcinoma		3 (11)
Target Lesion Sum of Diameters (mm)		
Mean (SD)		61 (38)
Min, Max		10, 165
Number of Target & Non-Target Lesions (at Baseline)		
>3		17 (63)
Mean (Min, Max)		4 (1,9)

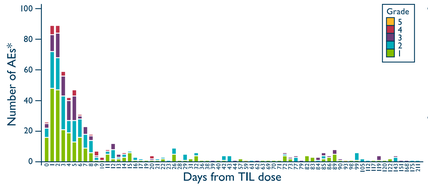
Table 2. Treatment Emergent Adverse Events (≥30%)

	N=27		
PREFERRED TERM	Any Grade, n (%)	Grade 3/4, n (%)	Grade 5, n (%)
Number of patients reporting at least one Treatment-Emergent AE	27 (100)	26 (96.3)	0
Chills	21 (77.8)	0	0
Anemia	15 (55.6)	15 (55.6)	0
Diarrhea	14 (51.9)	2 (7.4)	0
Pyrexia	14 (51.9)	1 (3.7)	0
Thrombocytopenia	14 (51.9)	12 (44.4)	0
Neutropenia	11 (40.7)	8 (29.6)	0
Vomiting	11 (40.7)	1 (3.7)	0
Hypotension	10 (37.0)	4 (14.8)	0
Dyspnea	9 (33.3)	1 (3.7)	0
Febrile neutropenia	9 (33.3)	8 (29.6)	0
Hypoxia	9 (33.3)	3 (11.1)	0
Leukopenia	9 (33.3)	6 (22.2)	0
Hypomagnesemia	8 (29.6)	0	0
Sinus tachycardia	8 (29.6)	0	0

*Patients with multiple events for a given preferred term are counted only once using the maximum grade under each preferred term. Treatment-Emergent Adverse Events refer to all AEs starting on or after the first dose date of TIL up to 30 days.

Figure 2. Adverse Events Over Time

Distribution of onset dates of AEs starting from TIL infusion until subsequent anti-cancer treatment or extraction date



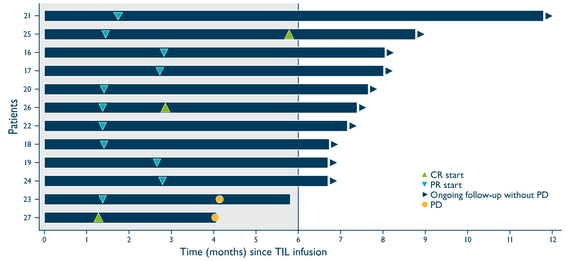
- The AE profile was generally consistent with the underlying advanced disease and the profile of the in line with lymphodepletion & IL-2 regimens
- Frequency of AEs over time is reflective of potential benefit of one time treatment with LN-145

*The number of AEs is cumulative and represent the total number of patients dosed

Table 3. Efficacy

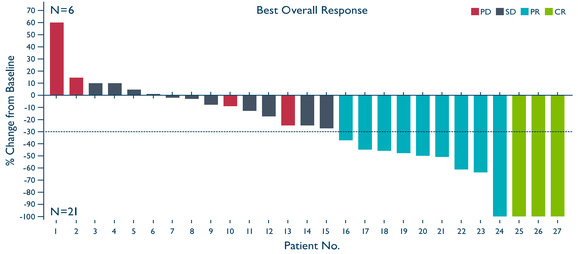
RESPONSE (RECIST v1.1)	PATIENTS, N=27 n (%)
Objective Response Rate (ORR)	**12 (44.4%)**
Complete Response (CR)	3 (11.1%)
Partial Response (PR)	9 (33.3%)
Stable Disease (SD)	11 (40.7%)
Progressive Disease (PD)	4 (14.8%)
Non-Evaluable	0
Disease Control Rate (DCR)	23 (85.2%)
Median Duration of Response (DOR)	**Not Reached**
Min, Max (range)	2.6+ to 9.2+ months

Figure 3. Time to First Response, Duration of Response, Time on Efficacy Assessment



- Mean time to first response 1.9 months
- Mean time to best response 2.4 months

Figure 4. Efficacy: Best Overall Response



- 78% of patients had a reduction in tumor burden
- Median follow up is 7.4 months
- Mean number of TIL cells infused: 28 x 10^9
- Median number of IL-2 doses administered was 6.0

CONCLUSIONS

- There is a high unmet medical need for effective treatments for patients with recurrent, metastatic, or persistent cervical cancer
- In previously treated cervical cancer patients, LN-145 TIL therapy results in
  - 11% CR
  - 44% ORR
  - 85% DCR
  - Acceptable safety and efficacy profile
- At median follow up of 7.4 months the median DOR has not been reached:
  - range 2.6+ to 9.2+ months

LN-145 autologous TIL has demonstrated potential efficacy for patients with cervical carcinoma and represents a viable therapeutic option warranting further investigation

DISCLOSURE
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