Interim Clinical Update of the Phase 1b Trial of ATRC-101 as Monotherapy or in Combination With Pembrolizumab for Select Advanced Solid Tumors

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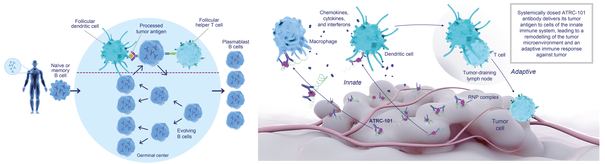
Background

- ATRC-101, an engineered monoclonal antibody identified via the Atreca discovery platform, targets a tumor-specific ribonucleoprotein complex and acts via a novel mechanism of action
- ATRC-101 stimulates innate and adaptive immune activity against tumors and changes the immune cell profile of the tumor microenvironment and blood in animal models[1-3]

Figure 1: Atreca discovery platform leverages B cell biology and ATRC-101 represents the potential of this approach

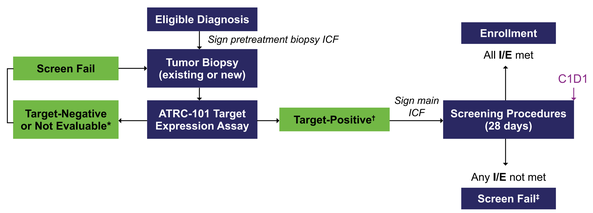


B cell response triggered by a cancer antigen is similar to those driven by antigens in infectious disease or autoimmunity.

Methods

- ATRC-101-A01 is an ongoing FIH dose escalation and expansion trial in participants with advanced solid tumors
- ATRC-101 is administered as monotherapy (Q3W or Q2W) or in combination with pembrolizumab (Q3W) until unacceptable toxicity or disease progression[4]
- Participants in the pembrolizumab cohort must have had suboptimal response to prior or ongoing PD-1/PD-L1 targeted therapy
- Simon 2-Stage design with ATRC-101 target-enriched expansion cohorts
- Results are presented as of the data cutoff of February 15, 2022

Figure 2. Pretreatment biopsy workflow for target-enriched cohorts



*A patient with target-negative or not-evaluable result may submit another biopsy obtained at a later timepoint. †Target-positive status assessed in a pretreatment tumor biopsy. ‡If a patient is deemed ineligible, the screening procedures may be repeated if the investigator believes there has been a change in eligibility status.

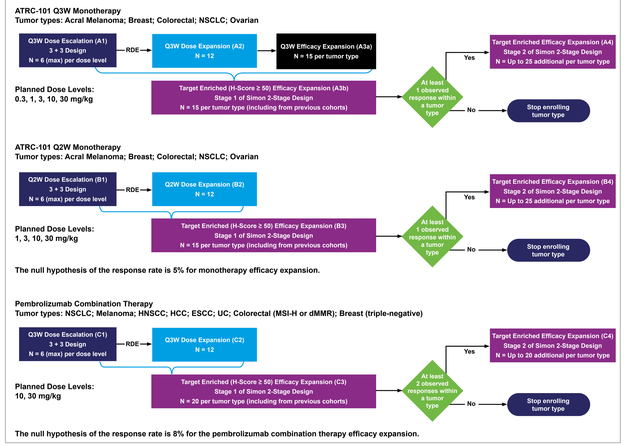
- An IHC assay was developed to detect ATRC-101 target immunoreactivity in FFPE tumor tissue sections and validated under CAP-CLIA
- Enrollment in target-enriched cohorts is restricted to participants with a pretreatment tumor biopsy, archival or fresh, demonstrating ATRC-101 target expression, H-Score ≥ 50, by IHC at a central laboratory
- For participants described herein, target expression was analyzed retrospectively

Key objectives

- Safety (primary), pharmacokinetics, immunogenicity, RP2D, and anti-tumor activity (RECIST v1.1)
- Biomarker analyses include IHC for target expression and CD8$^+$ T cell infiltration in baseline and on-treatment tumor biopsies

Methods (continued)

Figure 3: Simon 2-Stage multiple expansion cohort re-design of the study



Results

Table 1. Baseline characteristics of participants

Baseline characteristics	Overall (N = 50)	Q3W-Monotherapy (n = 37)	Q2W-Monotherapy (n = 9)	Q3W-Pembro (n = 4)
Age, median years (range)	58 (27–79)	62 (27–79)	53 (50–74)	56 (41–78)
ECOG PS at baseline, n (%)				
0	17 (34)	14 (37.8)	2 (22.2)	1 (25)
1	33 (66)	23 (62.2)	7 (77.8)	3 (75)
Cancer type, n (%)				
Colorectal	24* (48.0)	16 (43.2)	8* (88.9)	0
Breast	8 (16)	8 (21.6)	0	–
Ovarian	7 (14)	6 (16.2)	1 (11.1)	–
NSCLC	5 (10)	5 (13.5)	0	0
Melanoma	3 (6)	2 (5.4)	0	1 (25)
HNSCC	2 (4)	–	–	2 (50)
Urothelial	1 (2)	–	–	1 (25)
HCC	0	–	–	0
ESCC	0	–	–	0
Lines of prior cancer medications, median (range)	4.7 (1–9)	4.9 (1–9)	4.8 (1–7)	3.5 (2–5)
Prior therapy with checkpoint inhibitor, n (%)	23 (46)	17 (45.9)	2 (25)	4 (100)

*Includes 1 duodenal adenocarcinoma, enrolled in error.

Table 2. Analysis subsets

Analysis subsets	Overall	Q3W-Monotherapy	Q2W-Monotherapy	Q3W-Pembro
Safety* set, n	**50**	**37**	**9**	**4**
H-score† set, n (%)	36 (72)	28 (76)	5 (56)	3 (75)
Relevant dose (3-10-30 mg/kg) set, n (%)	**38 (76)**	**30 (81)**	**5 (56)**	**3 (75)**
Target lesion assessment‡ set, n (%)	32 (64)	25 (68)	4 (44)	3 (75)
Target lesion assessment‡ & H-score set, n (%)	25 (50)	20 (54)	2 (22)	3 (75)
Response§ & H-score set, n (%)	24 (48)	19 (51)	2 (22)	3 (75)

*Defined as number of participants who have received at least one dose. †Defined as successful determination of H-score in a pre-treatment biopsy within the safety set. ‡Defined as ≥ 1 post-baseline tumor assessment within the 3-10-30 mg/kg set. §Defined as ≥ 1 post-baseline overall response assessment within the 3-10-30 mg/kg set.

Note: Data for 3 additional participants dosed prior to February 15, 2022 was logged in the clinical database after the March 2022 data disclosure.

Results (continued)

Safety

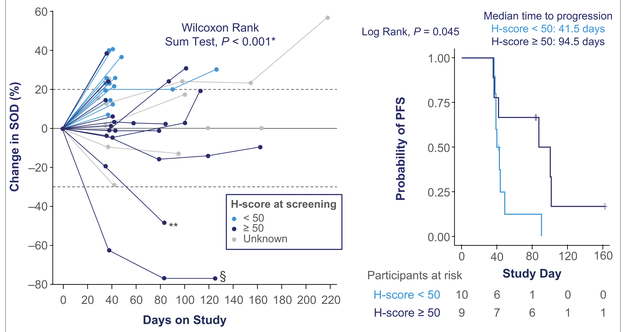
Table 3. Cumulative safety data as of February 15, 2022

N = 50	Q3W-Monotherapy					Q2W-Monotherapy			Q3W-Pembro	
ATRC-101 dose, mg/kg	0.3	1	3	10	30	1	3	10	10	30
n	3	3	9	7	15	3	3	3	3	1
Number of cycles	11	7	37	18	47	8	14	8	12	1
Participants with ≥ 1 TEAE, n (%)	3 (100)	3 (100)	9 (100)	7 (100)	13 (86.7)	3 (100)	3 (100)	3 (100)	3 (100)	1 (100)
Participants with ≥ 1 grade ≥ 3 TEAE, n (%)	1 (33.3)	1 (33.3)	3 (33.3)	2 (28.6)	0	1 (33.3)	0	1 (33.3)	0	0
Participants with ≥ 1 grade ≥ 3 treatment-related TEAE, n (%)	0	0	2 (22.2)[a]	1 (14.3)[b]	0	0	0	0	0	0

[a]Preferred terms for grade ≥ 3 treatment-related TEAEs – tumor pain and headache. [b]Preferred term for grade ≥ 3 treatment-related TEAE – small-intestinal obstruction.

Efficacy

Figure 4. Change in SOD of target lesions (% of baseline) per RECIST v1.1 (left) and probability of PFS (right)



*Wilcoxon Rank Sum Test on best change, H-Score < 50 vs ≥ 50. **PR participant (NSCLC) in Q3W monotherapy. §CR participant (melanoma) in ATRC-101 + pembrolizumab cohort.

Figure 5. Best RECIST v1.1 response by ATRC-101 target expression

*One participant not included that had target lesion measurements but no overall response data available.

Results (continued)

Pharmacokinetics

- Pharmacokinetics appear to be dose-proportional. Analyses of treatment-associated changes in the composition of CD3$^+$, CD4$^+$, and CD8$^+$ T cells in the blood is ongoing[4]

Enrollment

- Dose escalation has been completed
- Enrollment is continuing for the ATRC-101 monotherapy and pembrolizumab combination expansion cohorts (30 mg/kg, Q3W)
- Enrollment in specific expansion cohorts now requires pretreatment tumor biopsies demonstrating ATRC-101 target expression, H-score ≥ 50 by IHC
- More sites are being added to increase recruitment and enrollment

Conclusions

ATRC-101, without and with pembrolizumab, has been well tolerated by heavily pretreated participants

- No DLTs observed in participants enrolled in ATRC-101 monotherapy (Q2W or Q3W) or pembrolizumab combination cohorts
- No adverse events leading to treatment discontinuation or dose reduction

ATRC-101 has demonstrated anti-tumor activity in target expressers

- Higher ATRC-101 target expression at screening significantly associated with CR + PR + SD responses
- H-score ≥ 50 at screening delineates group in which ATRC-101 is most likely to exert maximum anti-tumor activity

ATRC-101 anti-tumor activity was observed in monotherapy and combination cohorts

- **CR** achieved in a target-expressing participant with melanoma in ATRC-101 (10 mg/kg Q3W) + pembrolizumab cohort
- **PR** achieved in a target-expressing participant with NSCLC in ATRC-101 monotherapy (30 mg/kg Q3W) cohort
- 67% of participants with high target expression treated with relevant ATRC-101 doses achieved SD or better

References

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Abbreviations

C1D1, cycle 1 day 1; CAP-CLIA, College of American Pathologists Clinical Laboratory Improvement Amendments regulations; CD, cluster of differentiation; CR, complete response; DLT, dose-limiting toxicity; dMMR, deficient mismatch repair; ECOG PS, Eastern Cooperative Oncology Group performance status; ESCC, esophageal squamous cell carcinoma; HNSCC, head and neck squamous cell carcinoma; ICF, informed consent form; I/E, inclusion/exclusion criteria; IHC, immunohistochemistry; FIH, first-in-human; FFPE, formalin-fixed paraffin-embedded; MSI-H, microsatellite instability-high; MTD, maximum tolerated dose; NSCLC, non-small cell lung cancer; PD, progressive disease; PD-1, programmed death-1; PD-L1, programmed death-ligand 1; PFS, progression-free survival; PR, partial response; Q2W, every 2 weeks; Q3W, every 3 weeks; RDE, recommended dose for expansion; RECIST, Response Evaluation Criteria in Solid Tumors; RNP, ribonucleoprotein; RP2D; recommended phase 2 dose; SD, stable disease; SOD, sum of diameters; TEAE, treatment-emergent adverse event; UC, urothelial carcinoma.

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