Phase I Dose-finding Study of MIW815 (ADU-S100), an Intratumoral STING Agonist, in Patients With Advanced Solid Tumors or Lymphomas

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Disclosures

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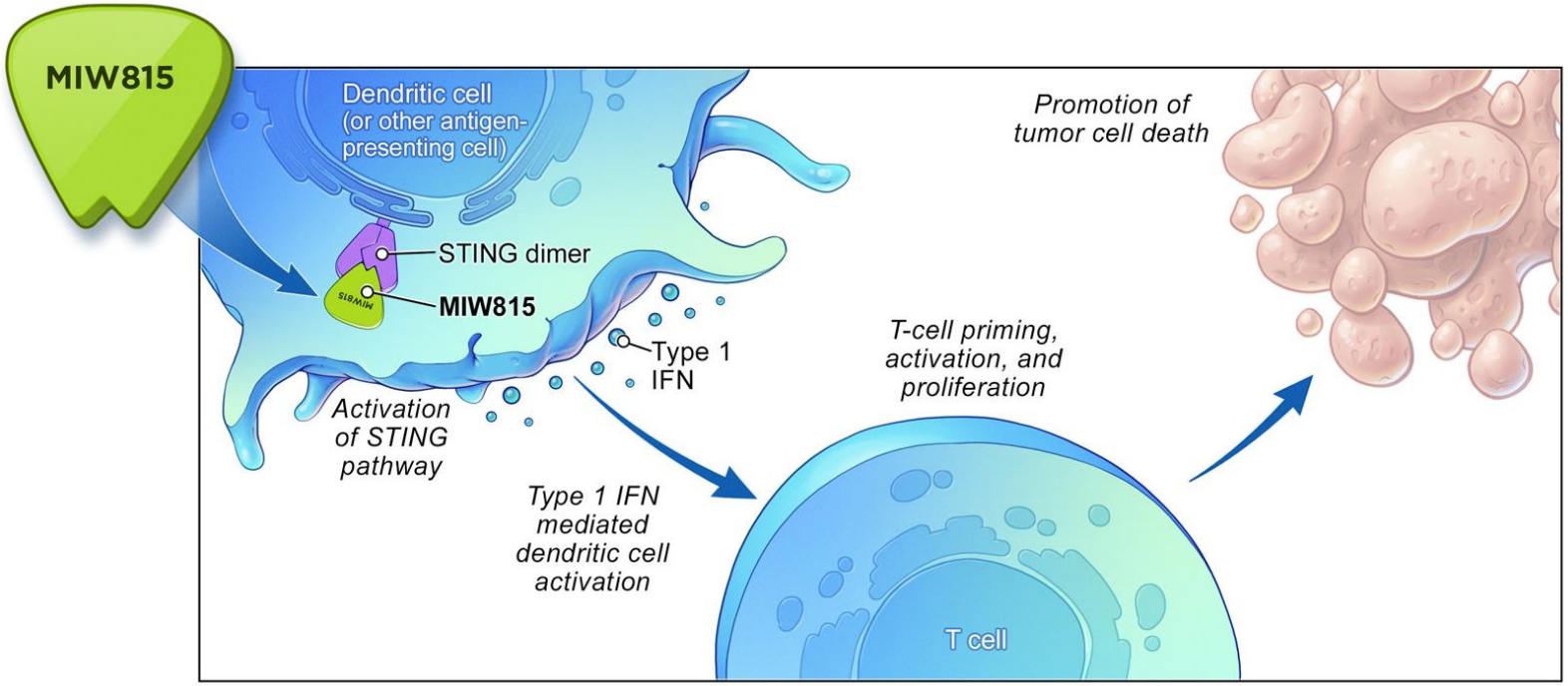
Introduction



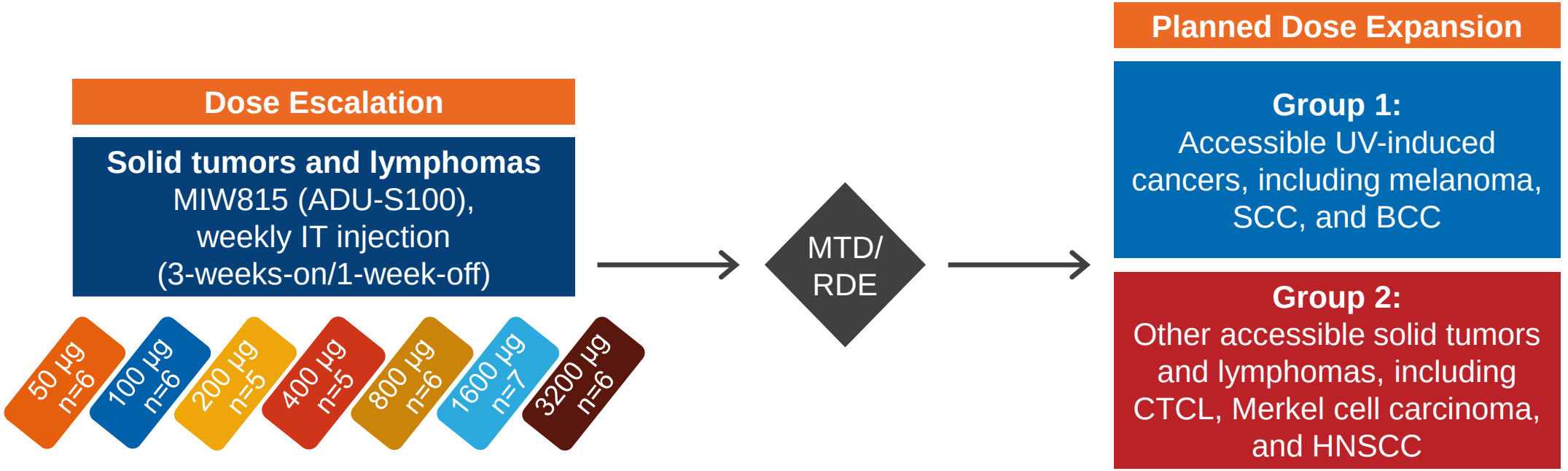
- The STING pathway plays a crucial role in the innate immune response to immunogenic tumors
  - Activation of the STING pathway increases IFN-β production and induces the recruitment and priming of CD8-positive T cells against tumor antigens[1]
- MIW815 (ADU-S100) is a novel synthetic cyclic dinucleotide that activates the STING pathway *in vitro*[2]
- In preclinical tumor mouse models, intratumoral injection of MIW815 (ADU-S100) resulted in tumor regression in both injected and non-injected lesions[3]

CD, cluster of differentiation; IFN, interferon; STING, stimulator of interferon genes.

1. Woo SR, et al. *Immunity* 2014;41:830–842; 2. Glickman LH, et al. *Cancer Res* 2016;76(14 Suppl):abst 1445; 3. Corrales L, et al. *Cell Rep* 2015;11:1018–1030.

Study Design

First-in-human Phase I study to evaluate the safety and efficacy of MIW815 (ADU-S100) in patients with advanced solid tumors or lymphomas



Study objectives

- **Primary:** Safety, tolerability, and recommended dose for future studies
- **Secondary:** PK, PD, and preliminary efficacy
- **Exploratory:** Biomarkers of response

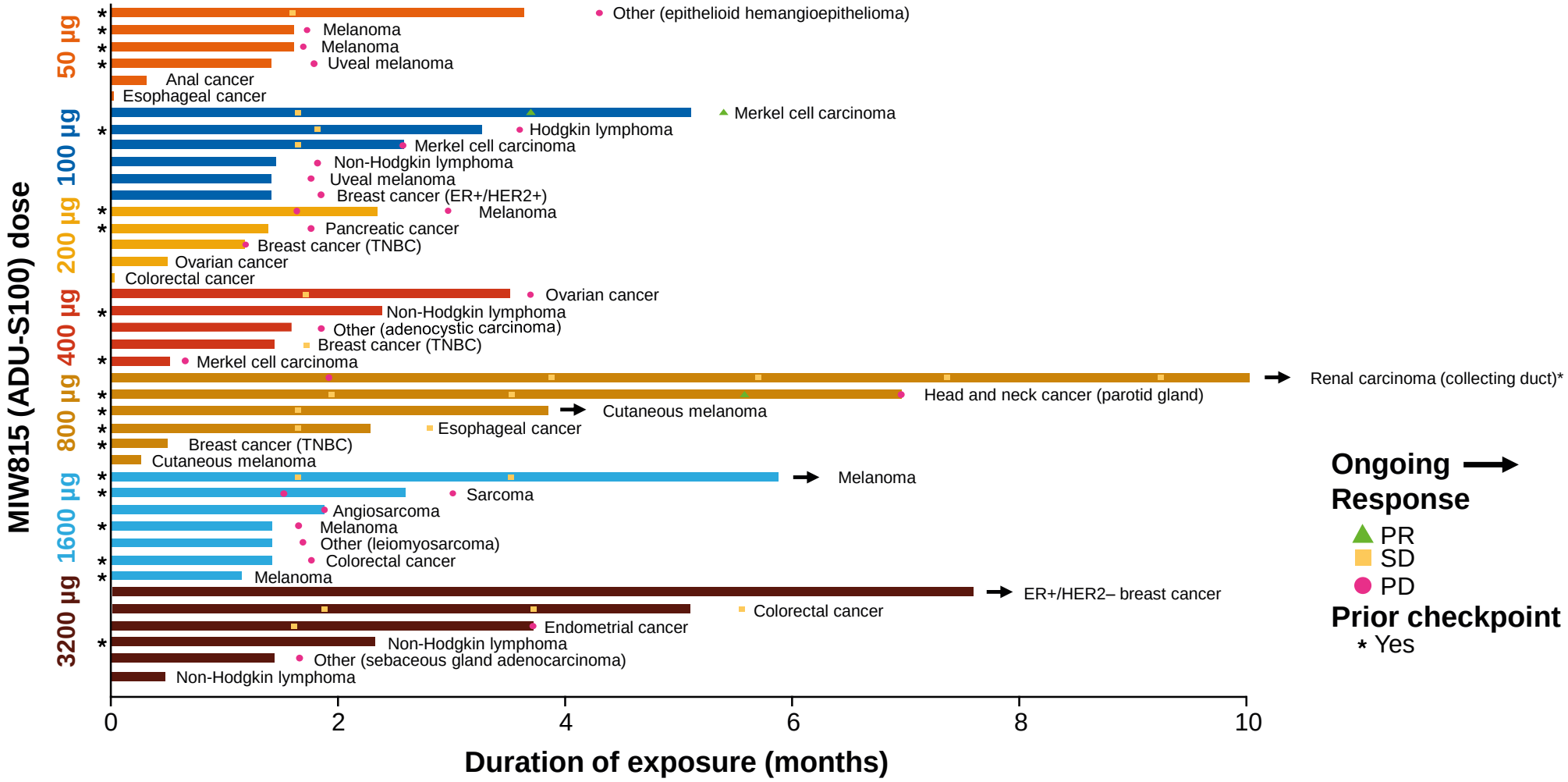
BCC, basal cell carcinoma; CTCL, cutaneous T-cell lymphoma; HNSCC, head and neck squamous cell carcinoma; IT, intratumoral; MTD, maximum tolerated dose; PD, pharmacodynamics; PK, pharmacokinetics; RDE, recommended dose for expansion; SCC, squamous cell carcinoma; UV, ultraviolet.

Safety and tolerability of MIW815 (ADU-S100)

- AEs suspected to be related to MIW815 (ADU-S100) treatment were reported in 78.0% of patients; 12.2% of patients experienced G3/4 AEs
  - The most common suspected related AEs (in ≥10% of all patients) were headache, injection site pain, and pyrexia (in 14.6% of patients each)
  - Elevated lipase was the only G3/4 suspected related AE reported in >1 patient (n=2; 4.9%)
- Treatment-emergent serious AEs were reported in 1 patient (G3 dyspnea and G4 respiratory failure; dose level: 1600 µg); this was related to underlying disease progression
- There were no DLTs observed during the first cycle of treatment
- No patients discontinued treatment due to an AE

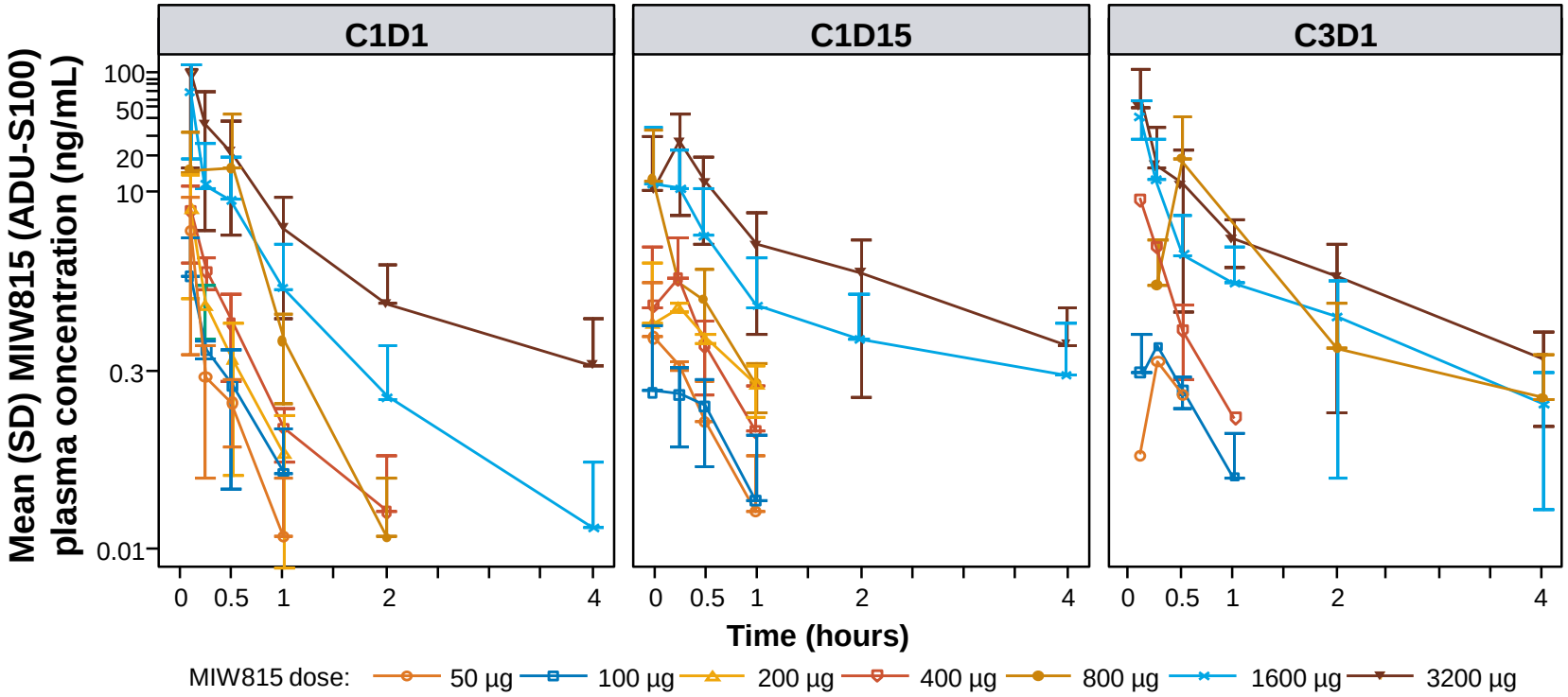
AE, adverse event; DLTs, dose-limiting toxicities; G, grade.

Time on MIW815 (ADU-S100) Treatment and Response Evaluation



Data cut-off: August 16, 2018.
*Patient ongoing treatment at 13 months.
ER+, estrogen receptor-positive; HER2–, human epidermal growth factor receptor 2-negative; HER2+, HER2-positive; PD, progressive disease; PR, partial response; SD, stable disease; TNBC, triple-negative breast cancer.

Pharmacokinetics of MIW815 (ADU-S100)

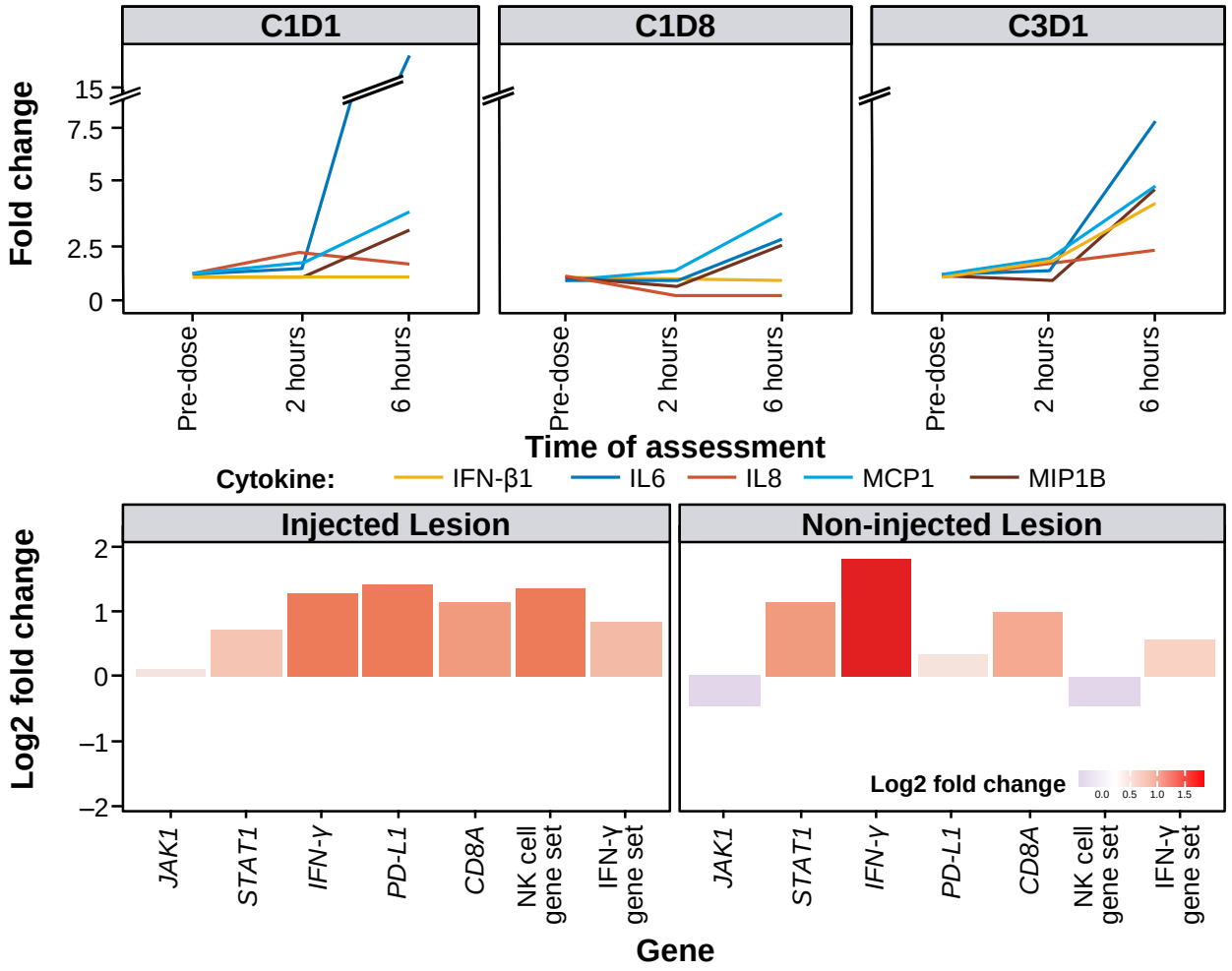


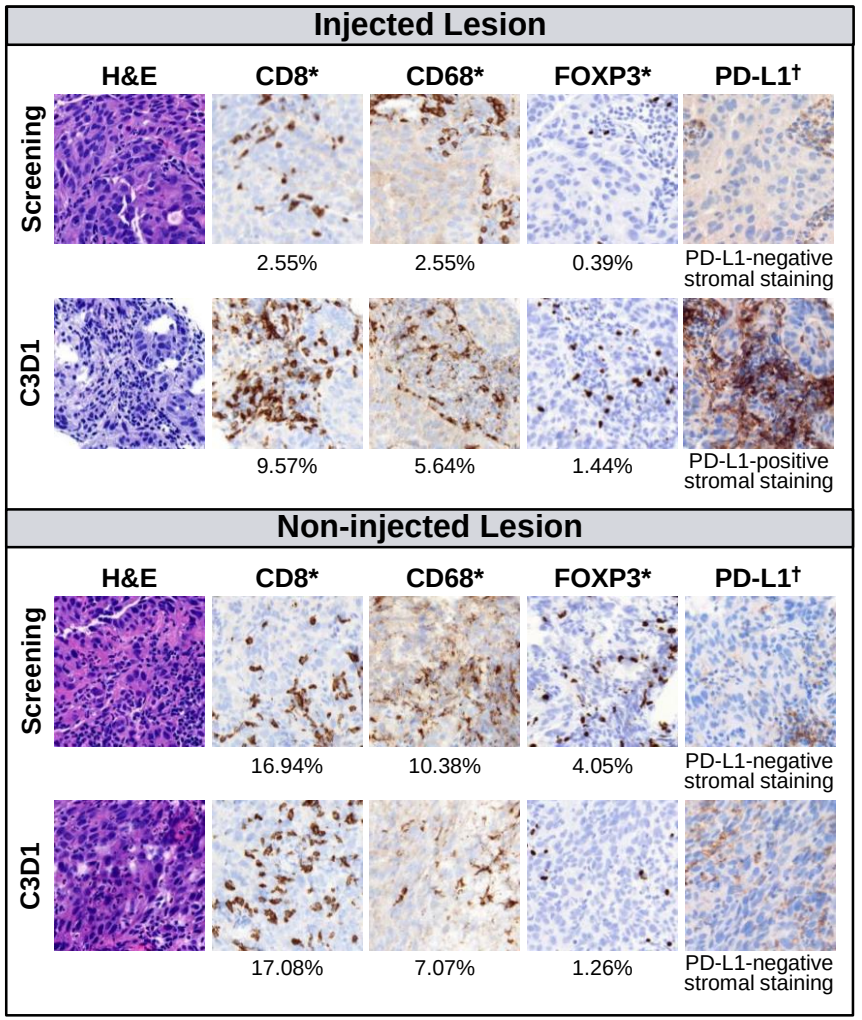
- MIW815 (ADU-S100) was rapidly absorbed, reaching maximal plasma concentration within minutes of dosing
- Exposure increased in a dose-dependent manner
- MIW815 (ADU-S100) had an observed terminal half-life of 10–23 minutes

Data cut-off: August 16, 2018.
C, cycle; D, day; SD, standard deviation.

Case example

Pre- and Post-MIW815 (ADU-S100) Therapy Cytokine Levels, RNA, and IHC in a Patient With Collecting Duct Carcinoma





*Biomarker area % per image analysis; †TPS % per pathologist analysis; PD-L1 measured using the IHC 22C3 pharmDx assay.
C, cycle; CD, cluster of differentiation; D, day; FOXP3, forkhead box P3; H&E, hematoxylin and eosin; IFN, interferon; IHC, immunohistochemistry; IL, interleukin; *JAK1*, Janus kinase 1; MCP1, monocyte chemoattractant protein 1; MIP1B, macrophage inflammatory protein 1 beta. NK, natural killer; PD-L1, programmed death-ligand 1; *STAT1*, signal transducer and activator of transcription 1; TPS, tumor positive score.

Conclusions

- Single-agent MIW815 (ADU-S100) was well tolerated at doses ranging from 50 to 3200 µg in patients with advanced solid tumors and lymphoma with no DLTs noted. Dose escalation is ongoing
- Preliminary signs of MIW815 (ADU-S100) biological activity were observed in patients with advanced solid tumors and lymphoma, including those who had previously received treatment with a checkpoint inhibitor
- In the highlighted patient case, the ability of MIW518 (ADU-S100) to activate the antitumor immune response is suggested by observed increases in CD8-positive TILs, genes involved in the antitumor immune response, and systemic cytokines following MIW815 (ADU-S100) injection
- MIW815 (ADU-S100) is currently being investigated in combination with anti-PD-1 (NCT03172936) and anti-CTLA-4 (NCT02675439) antibodies in Phase I clinical trials in patients with advanced solid tumors and lymphomas

CD, cluster of differentiation; CTLA-4, cytotoxic T-lymphocyte–associated antigen 4; DLT, dose-limiting toxicity; PD-1, programmed cell death protein 1; TIL, tumor-infiltrating lymphocyte.

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