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Off-the-shelf CAR T: Pioneering an Off-the-Shelf, Allogeneic T-cell Platform

SITC Adoptive Cellular Therapies Workshop
September 5, 2019

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Nasdaq: ATRA

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Innovative Off-the-Shelf, Allogeneic T-Cell Platform

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State-of-the-Art T-Cell Manufacturing

- Dedicated, expandable ATOM (Atara T-cell Operations & Manufacturing) facility in Thousand Oaks, CA
- Flexibility to produce multiple T-cell and CAR T immunotherapies
- Integrated research and process science to enable rapid development and leverage research collaborations
- Designed to global regulatory standards (completed licensure for clinical production)

Pioneering Off-the-Shelf, Allogeneic T-Cell Immunotherapies

Three strategic priorities to create value

Tab-cel® (tabelecleucel)

Multiple sclerosis

Next-gen CAR T

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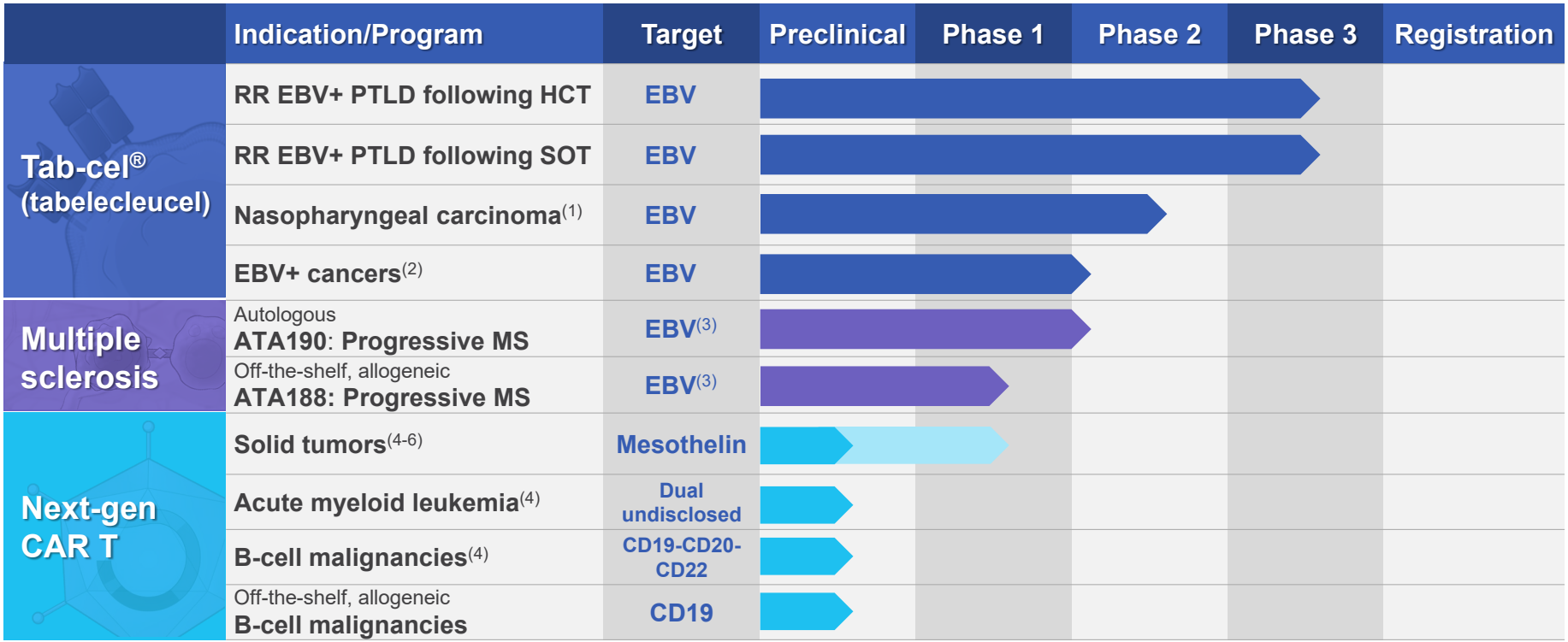
Robust T-Cell Immunotherapy Pipeline



EBV+ PTLD: EBV-Associated Post-Transplant Lymphoproliferative Disease; RR: rituximab relapsed/refractory; HCT: allogeneic hematopoietic cell transplant; SOT: solid organ transplant
Other programs: ATA230 (CMV), ATA368 (HPV), ATA520 (WT1) and ATA621 (BK/JCV)

(1) Phase 1b/2 study in combination with anti-PD-1 therapy, KEYTRUDA® (pembrolizumab), in patients with platinum-resistant or recurrent EBV-associated NPC.
(2) Phase 2 multi-cohort study planned with possible indications including EBV+ PTLD with CNS involvement, EBV+ PID/AID LPD, EBV+ LMS and other potential EBV-associated diseases
(3) Targeted antigen recognition technology
(4) Development expected to start in autologous setting
(5) Mesothelin is expressed at high levels on the surface of cells in aggressive solid tumors including mesothelioma, triple-negative breast cancer, esophageal cancer, pancreatic cancer and non-small cell lung cancer
(6) MSK investigator-sponsored Phase 1 study (NCT02414269) of a mesothelin-targeted CAR T immunotherapy is ongoing; Atara's CAR T collaboration with MSK will focus on development of a next-generation, mesothelin-targeted CAR T using novel 1XX CAR signaling and PD-1 dominant negative receptor (DNR) checkpoint inhibition technologies.

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Pioneering Off-the-Shelf, Allogeneic T-Cell Immunotherapies

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Tab-cel® (tabelecleucel)

EBV-associated cancers

FDA breakthrough designation & EMA PRIME for EBV+ PTLD

Multiple sclerosis

Developing first T-cell immunotherapy in autoimmune disease

Next-generation CAR T

Mesothelin-targeted CAR T immunotherapy for solid tumors

Off-the-shelf, allogeneic platform

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EBV+ PTLD: Epstein-Barr virus-associated post-transplant lymphoproliferative disease

EBV-Associated Post-Transplant Lymphoproliferative Disease
Aggressive, Often Deadly Cancer with No Approved Therapy

Rare B-cell lymphoma that occurs in immunosuppressed patients after transplant

Jessica
EBV+ PTLD champion

- Median age under 40 years vs. around 65 years for all lymphomas
  - **Bone marrow transplant (HCT)**
    EBV+ PTLD risk up to recovery of immune system (~1 year)
  - **Solid organ transplant (SOT)**
    Chronic risk of PTLD from immunosuppression; Highest risk within ~1 year of transplant(1)
- High mortality in rituximab ± chemo relapsed/refractory patients
  - **Median survival**
    HCT: under 1 month(2)
    SOT: 3-12 months(1,3)

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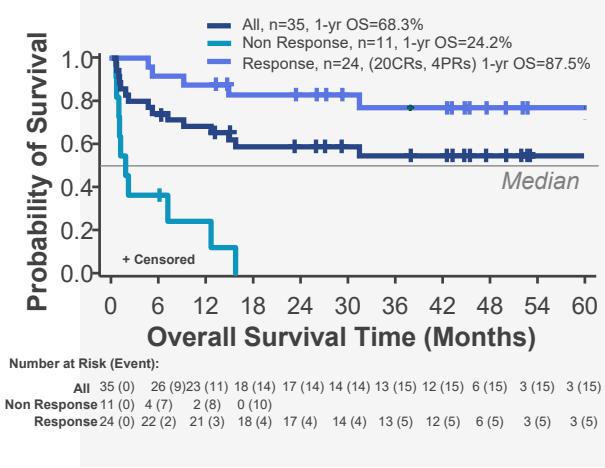
(1) Dierickx D, Habermann TM. *N Engl J Med*. 2018 Feb 8;378(6):549-562.
(2) Atara estimated 1-year survival based on analysis of Ocheni S, et al. 2008 Aug;42(3):181-6; Fox CP, *et al.* 2014;49(2):280-6.
(3) Choquet S, et al. 2007 Aug;86(8):599-607; Zimmermann, H, *et al.* Abstract PF719, EHA 2019.

Tab-cel® – Positive Long-Term Outcomes for Patients with EBV+ PTLD Observed in Phase 2 Studies(1)

HCT



Overall survival at 1 year

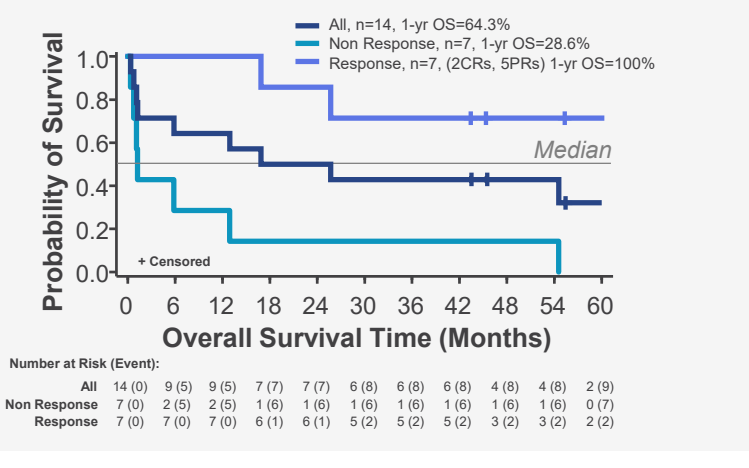
68%

Overall survival at 2 years in responders

83%

Median survival not yet reached(2)

SOT



Overall survival at 1 year

64%

Overall survival at 2 years in responders

86%

Median survival of 21.3 months

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Few treatment-related serious adverse events (SAEs): 12 possibly related Serious Adverse Events (SAEs) among 173 patients: no infusion related toxicities, no CRS (cytokine release syndrome) and three possibly related graft vs. host disease (GvHD); Safety data on file as of December 2017.

(1) NCT00002663 and NCT01498484; Prockop, S., *et al.* EHA 2018.

(2) after 23.3 months of follow-up

Pioneering Off-the-Shelf, Allogeneic T-Cell Immunotherapies

Three strategic priorities to create value

Tab-cel® (tabelecleucel)

EBV-associated cancers

FDA breakthrough designation & EMA PRIME for EBV+ PTLD

Multiple sclerosis

Developing first T-cell immunotherapy in autoimmune disease

Next-generation CAR T

Mesothelin-targeted CAR T immunotherapy for solid tumors

Off-the-shelf, allogeneic platform

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We Have Assembled a Tool Kit of Technologies Designed to Address Current CAR Limitations

1 Multi-Targeted CARs	2 Next Gen Co-stimulatory domains	3 PD1 Dominant Negative Receptor	4 Other Technologies
Methods of designing multi-targeted CAR T cells directed against two or more identified antigens	Novel CD28 and 4-1BB co-stimulatory domains which may offer more physiologic T cell signaling	Provide intrinsic checkpoint inhibition to unlock solid tumor microenvironment	Artificial antigen presenting cell technology optimizes manufacturing

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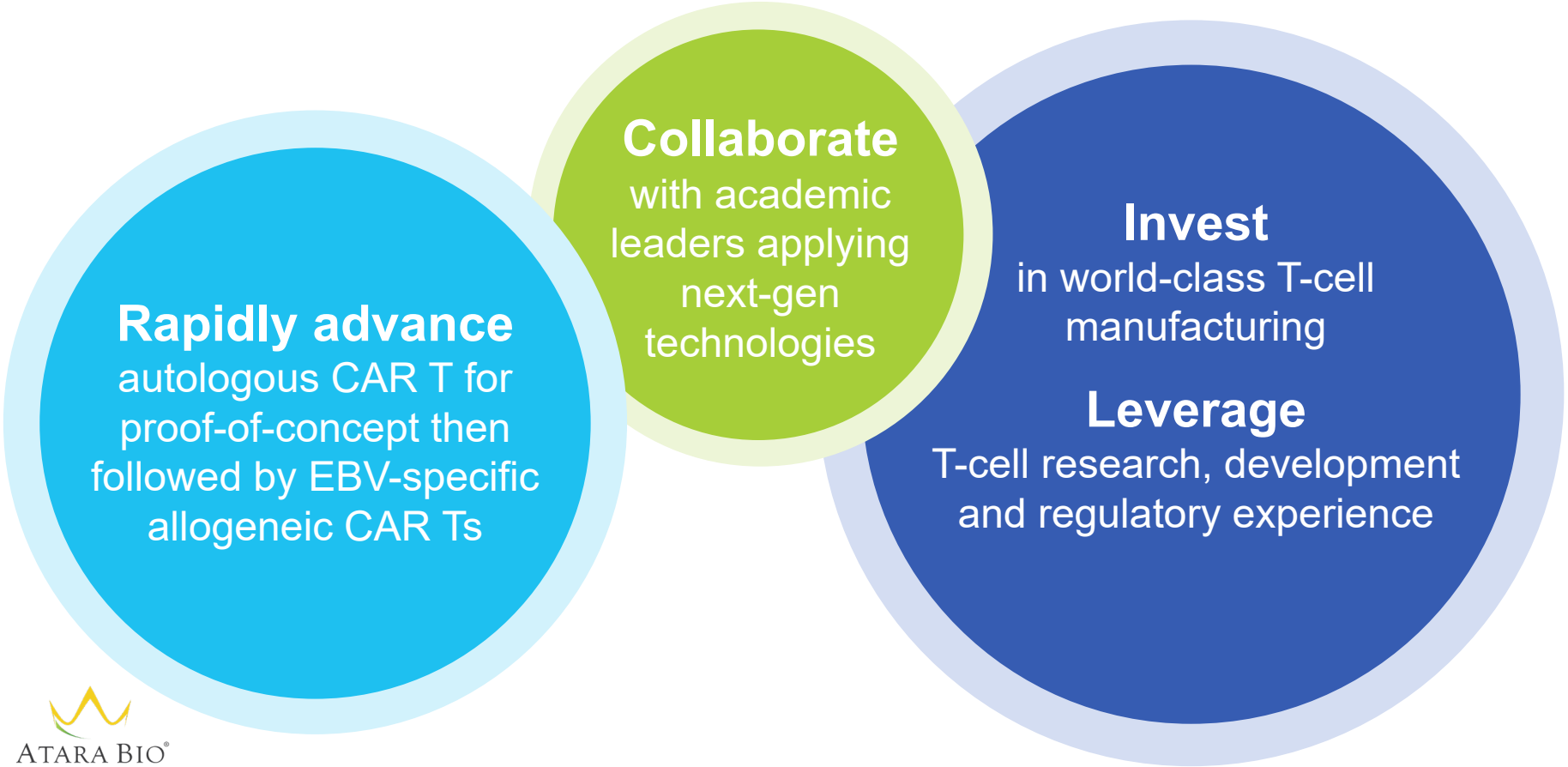
Atara's Next-Generation CAR T Immunotherapy Strategy



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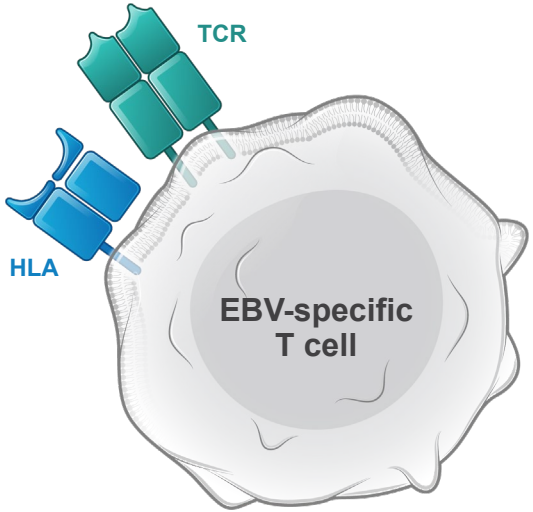
Advantages of EBV-Specific T-Cell Immunotherapy Platform



- EBV present in >95% of individuals by age 40
  - Implicated in a wide range of cancers and autoimmune diseases
  - EBV-specific T cells sourced from established healthy donor networks
- No gene editing or HLA edits required
  - Maintaining healthy donor T cell proliferation and persistence advantages
- Risk of GvHD may be reduced by EBV TCR specificity
- EBV T-cells may be immunologically privileged(1)
  - Long-term persistence when engineered to express an additional WT1 TCR(2)
  - Traffic to and embed within solid tumors where their activation can lead to antitumor activity(3)
  - Expand in immuno-competent patients without lymphodepleting chemotherapy pre-treatment(4)

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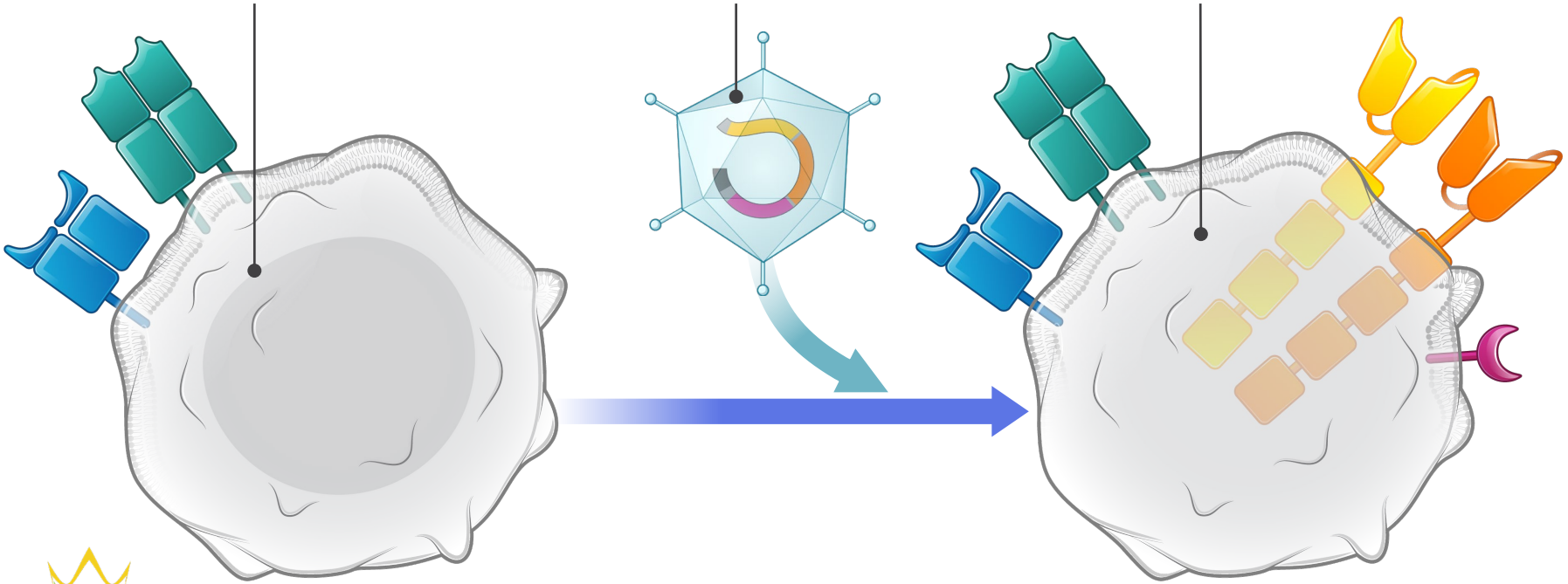
(1) Maeda Y, *et al*. *Science*. 2014 Dec 19;346(6216):1536-40; Regulatory T cells (T_{regs}) "silence" T cells with reactivity to self
(2) Chapuis AG, *et al.* Nat Med. 2019 Jul;25(7):1064-1072.
(3) Rosato P, *et al.* Nature Communications 2019 Feb 4; 10:567; Virus-specific memory T Cells populate tumors and can be repurposed for tumor immunotherapy.
(4) Prockop S, *et al.* Proc ASCO 2016.

Atara Next-Generation and Off-the-Shelf, Allogeneic CAR T Approach

1 EBV-specific off-the-shelf, allogeneic T cell platform

2 Next-generation CAR technologies

3 Off-the-shelf CAR T with broad applications



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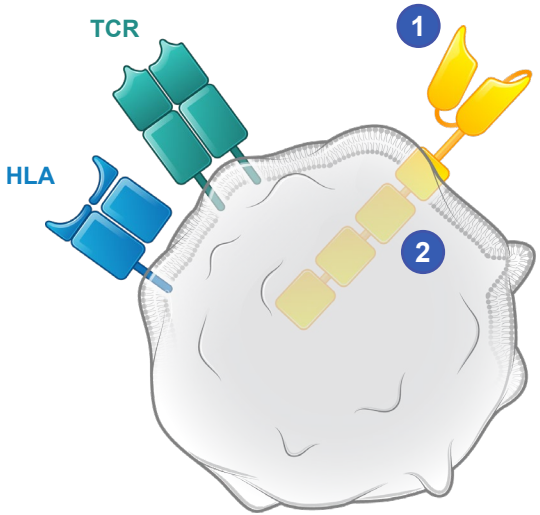
ATA3219: Off-the-Shelf, Allogeneic Next Gen CAR T Immunotherapy Targeting CD19



Key Technologies		
1	scFv	CD19 targeting scFv
2	Co-stimulatory domain	Novel costimulatory domain that may enhance CAR T cytotoxicity, proliferation and persistence

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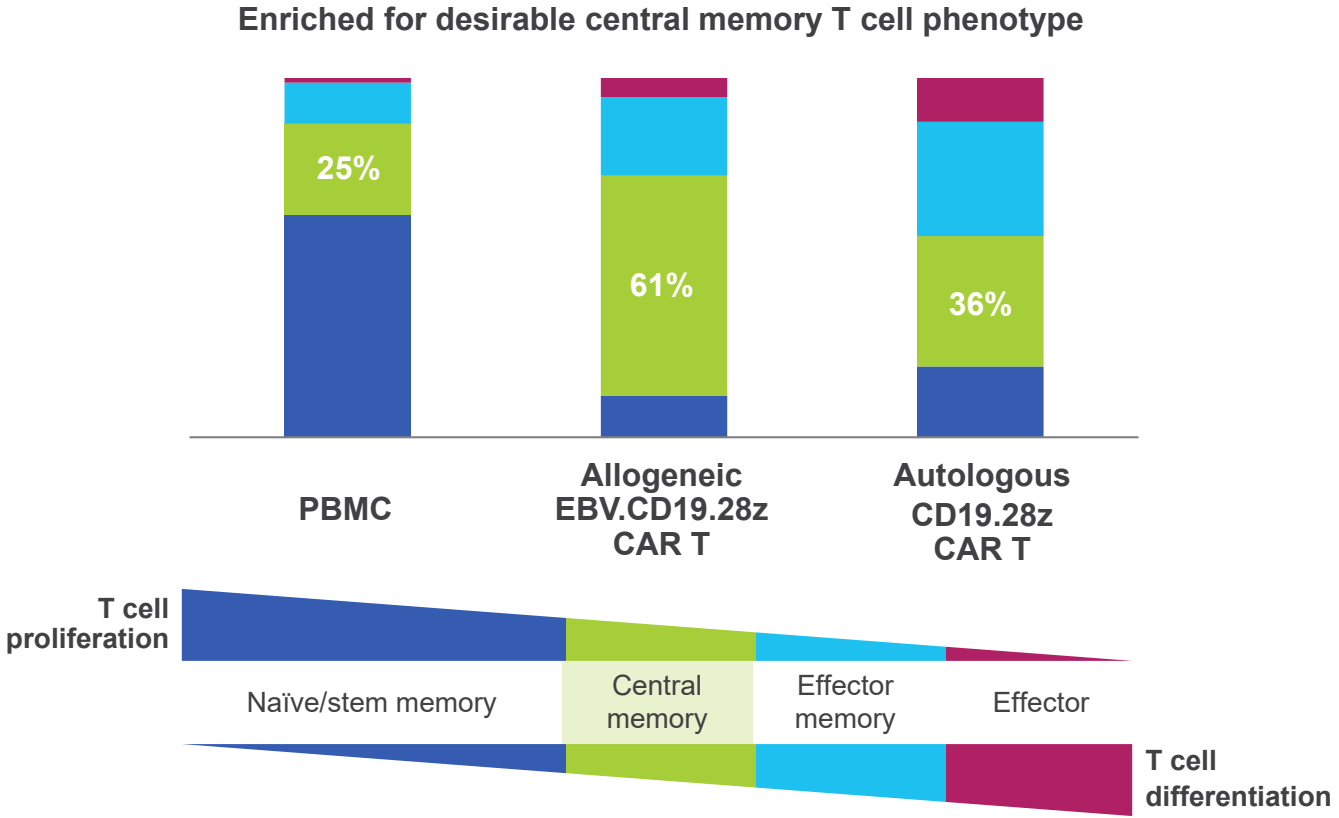
Atara Allogeneic EBV.CD19.28z CAR T Balances Proliferation Capacity and Activated T Cell Function

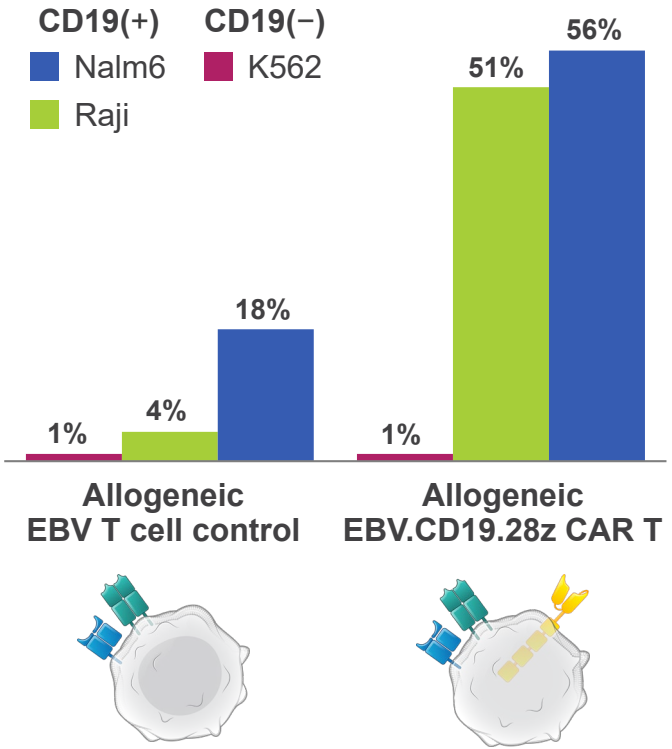


PBMC: Peripheral Blood Mononuclear Cell

Atara Allogeneic EBV.CD19.28z CAR T Demonstrates Potent *in vitro* CD19 Activity

Nalm6, Raji and K562 are the standard cells for CD19 CAR T positive and negative controls

- Left: EBV-specific T cells without CAR shows low activity for CD19(+) and CD19(−) cells
- Right: Allogeneic EBV.CD19.28z CAR T targets CD19(+) cells



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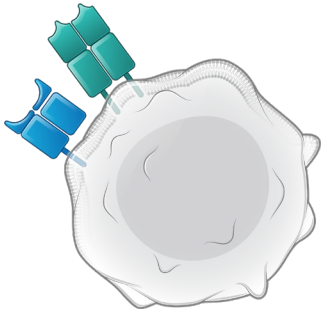
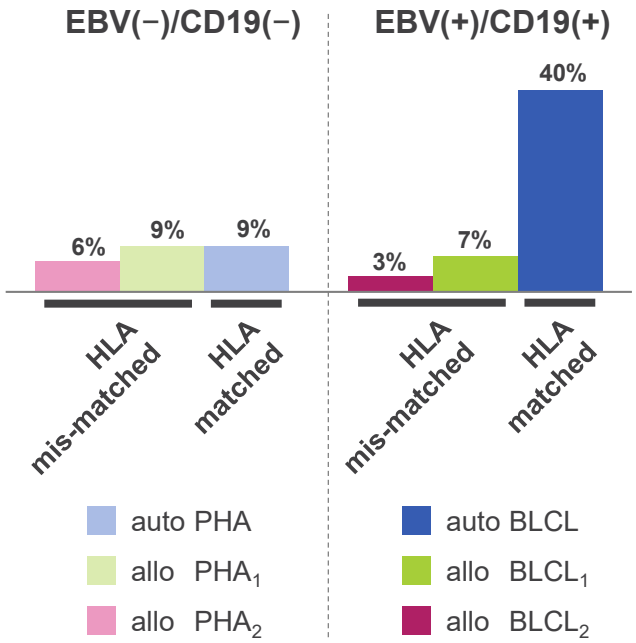
Atara Allogeneic EBV-Specific T Cells Require HLA Match

Low levels of off-target alloreactivity designed to minimize GvHD risk

Allogeneic EBV T cell control





HLA: Human Leukocyte Antigen
BLCL: EBV transformed B lymphoblastoid cell line
PHA: Phytohaemagglutinin Blast

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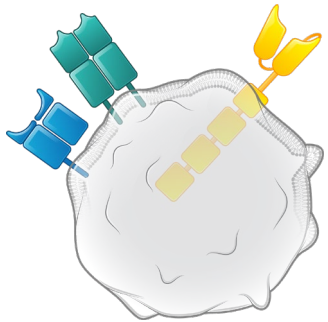
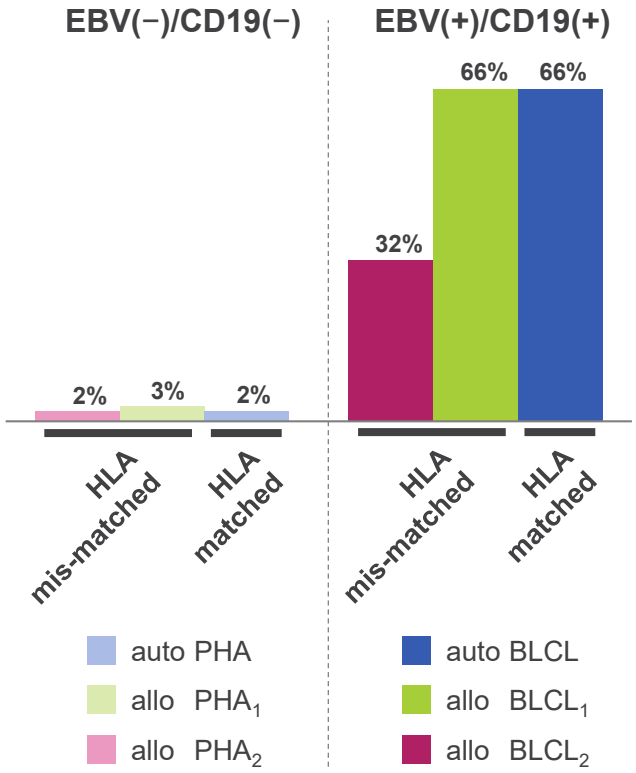
Atara Allogeneic EBV.CD19.28z CAR T Selectively and Specifically Targets CD19 Independent of HLA

Low levels of off-target alloreactivity maintained

Allogeneic EBV.CD19.28z CAR T





HLA: Human Leukocyte Antigen
BLCL: EBV transformed B lymphoblastoid cell line
PHA: Phytohaemagglutinin Blast

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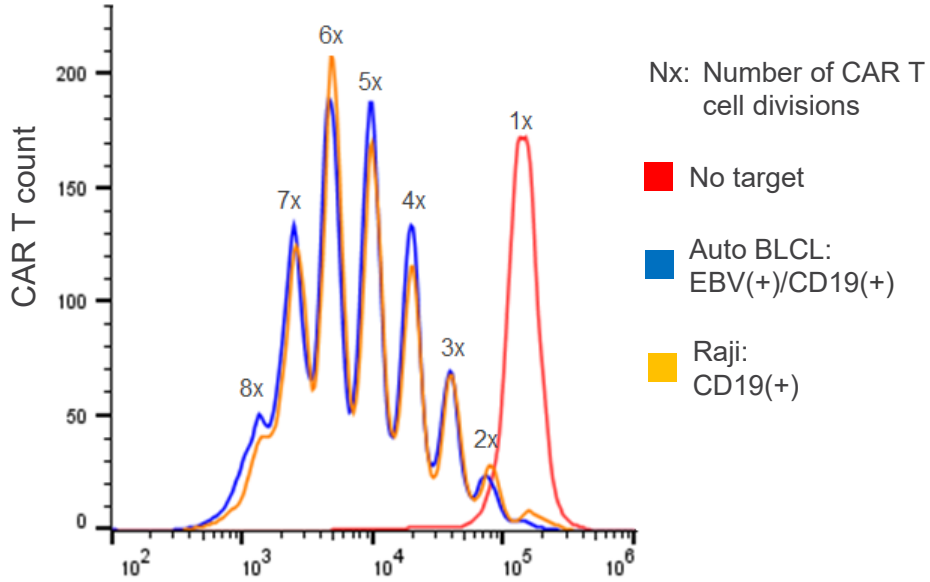
Atara Allogeneic EBV.CD19.28z CAR T Shows Strong Antigen-Specific Proliferation and Persistence

Robust multi-day proliferation following stimulation with CD19 and EBV/CD19 targets



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Atara Next Generation CAR T Platform – Conclusions and Next Steps

- Leverages innovative licensed technologies and EBV-specific T cell expertise
- Rapid ability to advance CAR T programs integrating research and process science under one roof (ATOM facility)
- EBV.CD19.28z CAR T demonstrates
  - High CAR transduction
  - Increased frequency of central memory T cell phenotype
  - Specific and selective CD19 activity
  - Low levels of off-target alloreactivity designed to minimize GvHD risk
  - Strong antigen-specific proliferation
- Developing an off-the-shelf, allogeneic CAR T targeting CD19 using next generation costimulatory domain (ATA3219)

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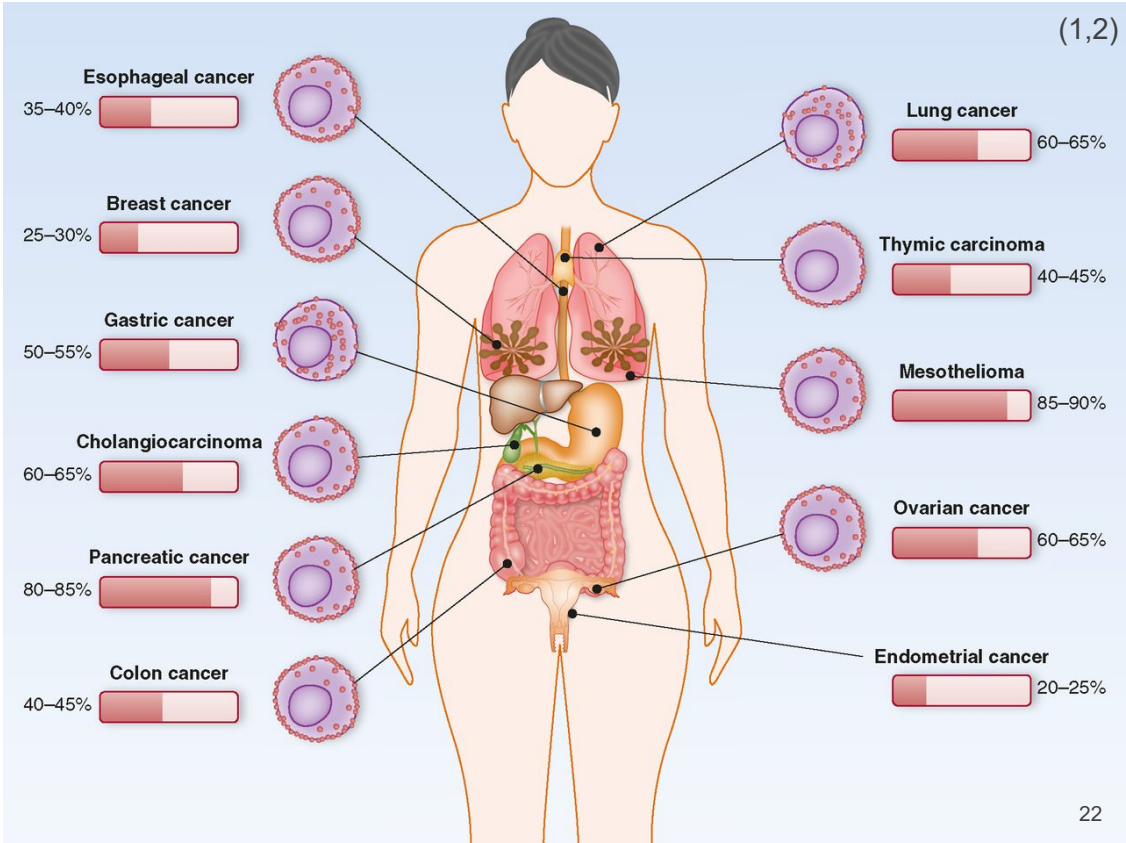
Licensed Mesothelin-Targeted CAR T Immunotherapy for Solid Tumors from Prasad Adusumilli's Lab at MSK

Mesothelin is an attractive target associated with aggressive solid tumors

- Aberrant mesothelin expression promotes cancer cell proliferation and confers resistance to apoptosis
  - Associated with mesothelioma, triple-negative breast cancer and non-small cell lung cancer
- Mesothelin-associated cancers(1)
  - Incidence: ~340,000 patients
  - Prevalence: ~2 million patients



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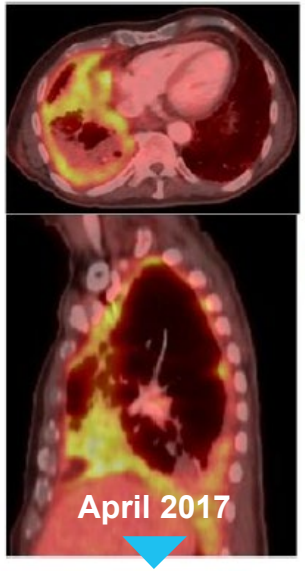
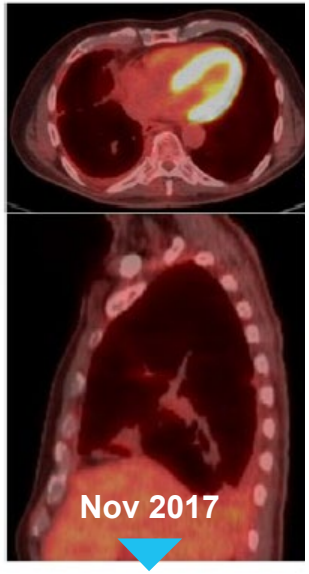
(1) Morello A, Sadelain M, Adusumilli PS. Mesothelin-Targeted CARs: Driving T Cells to Solid Tumors. *Cancer Discov.* 2016 Feb;6(2):133-46; U.S. incidence/prevalence.

(2) Frequency and distribution pattern of the mesothelin protein in solid malignancies.

Prioritized Mesothelin-Targeted Next-Generation CAR T
Positive MSK Phase 1 Results Support Autologous ATA2271 Program



73-year-old with unresectable biphasic mesothelioma(2)



Complete response after CAR T + PD-1;

No additional therapies for 16 mo

- Positive ASCO 2019 results from ongoing MSK Phase 1 study for mesothelin-targeted CAR T(1)
- 16 malignant pleural mesothelioma patients treated following preconditioning cyclophosphamide plus PD-1 and minimum follow-up time of 3 months
  - 80% overall survival (OS) at 12 months
  - 63% best overall response rate (ORR)
  - Three durable investigator assessed complete responses (CR)(3)
  - Seven partial responses (PR)
- Generally well-tolerated with no CAR T-related toxicities higher than grade 2
  - Unique scFv binds to mesothelin only above cancer threshold, avoiding major on-target, off-tumor toxicity

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(1) Adusumilli PS, *et al.* 2019 American Society of Clinical Oncology (ASCO) Annual Meeting oral presentation: Regional delivery of mesothelin-targeted CAR T cells for pleural cancers: Safety and preliminary efficacy in combination with anti-PD-1 agent. Abstract 2511, S406, Tuesday, June 4, 2019, 8:36 a.m. - 8:48 a.m. CDT, Chicago.
(2) PET CT results from ongoing MSK Phase 1 investigator-sponsored study (NCT02414269) patient provided for illustrative purposes only to show how clinical parameters above may correlate to clinical presentation of a patient
(3) Not based on RECIST/mRECIST

Next-Generation CAR T Oncology Pipeline Expanding with Novel Technology Collaborations

	Indication	Target	CAR T Technologies	
ATA2271	Solid tumors(1)	Mesothelin	PD-1 DNR Novel 1XX co-stimulation Autologous(2)	Memorial Sloan Kettering Cancer Center
ATA2321	AML	Dual-targeted undisclosed	Novel co-stimulation Autologous(2)	MOFFITT CANCER CENTER
ATA2431	B-cell malignancies	CD19-CD20-CD22	Novel co-stimulation Autologous(2)	MOFFITT CANCER CENTER
ATA3219	B-cell malignancies	CD19	Off-the-shelf, allogeneic Novel co-stimulation	ATARA BIO®

Prioritized the mesothelin-targeted next-generation CAR T program with an IND planned for autologous ATA2271 in advanced mesothelioma in 2020

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AML: acute myeloid leukemia; DNR: Dominant Negative Receptor

(1) Mesothelin is expressed at high levels on the surface of cells in aggressive solid tumors including mesothelioma, triple-negative breast cancer, esophageal cancer, pancreatic cancer and non-small cell lung cancer

(2) Development expected to start in autologous setting with option to develop in parallel or transition to an off-the-shelf, allogeneic product

Nasdaq:
ATRA

Thank you

ATARA BIO®

Ayden
EBV+ PTLD champion