Practical Aspects of Immunotherapy Management

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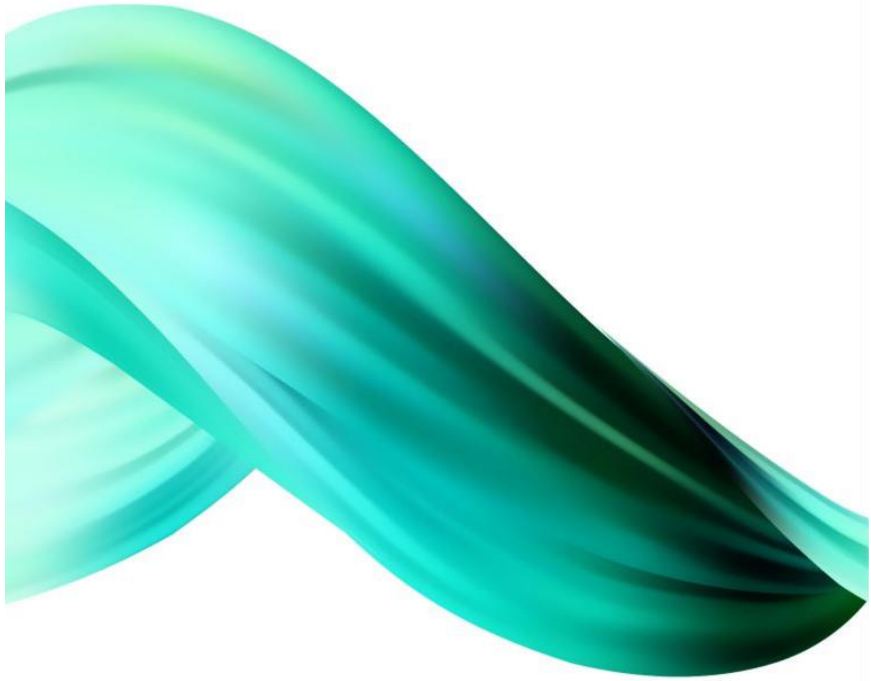

Disclosures

- No relevant financial relationships to disclose.

Agenda

- Preparation Before Treatment
- Follow-up After Treatment
- Common Outpatient Toxicities
- COVID Antibody Response and Vaccines
- Transition to Local Oncologist
- Financial Support

CAR-T: Preparation Before Treatment

- Social worker evaluation
  - Social support/living situation
  - Coping/mental health/substance abuse
  - Psychosocial restrictions
  - Financial assessment

CAR-T: Preparation Before Treatment

- Screening tests: labs, EKG, bone marrow biopsy
- Leukapheresis – may need central line (Quinton)
- Bridging therapy (chemo or XRT)
- Inpatient admission: Length of stay, COVID status
- Education – CRS and neurotoxicity
- Wallet card and CAR-T bracelet

Bispecific Antibodies: Preparation Before Treatment

- Screening tests
- Requires inpatient admission for first 1-3 doses
- No caregiver requirement
- Must comply with treatment – some weekly, every other week, etc.
- Education

CAR-T Follow-Up

- Clinic visits 2X/week for first 30 days
  - CRS/neurotoxicity assessment
- No driving, operating heavy machinery for 4 vs 8 weeks
- Neutropenic precautions
  - Dietary education
- UCSF ER first 30 days

Post treatment prophylaxis

- Antimicrobial prophylaxis
- Seizure prophylaxis – typically starts Day of CAR T
- B cell aplasia→ hypogammaglobulinemia
  - IVIG if IgG <400mg/dL

Toxicities: Cytopenias

- One of the most common toxicities we see within the first 1-3 months
- Manage and partner with outpatient MD
- Avoid GCSF initially in CAR-T patients
- Occasionally see neutropenia in bispecific antibody therapy

Toxicities: Cytopenias

Most Common Adverse Events

KarMMa™

AE,* n (%)	Ide-cel Treated (N=128)	
	Any Grade	Grade ≥3
Hematologic		
Neutropenia	117 (91)	114 (89)
Anemia	89 (70)	77 (60)
Thrombocytopenia	81 (63)	67 (52)
Leukopenia	54 (42)	50 (39)
Lymphopenia	35 (27)	34 (27)
Gastrointestinal		
Diarrhea	45 (35)	2 (2)
Nausea	37 (29)	0
Other		
Hypokalemia	45 (35)	3 (2)
Fatigue	43 (34)	2 (2)
Hypophosphatemia	38 (30)	20 (16)
Hypocalcemia	34 (27)	10 (8)
Pyrexia	32 (25)	3 (2)
Hypomagnesemia	30 (23)	0
Decreased appetite	27 (21)	1 (<1)
Headache	27 (21)	1 (<1)
Hypogammaglobulinemia	27 (21)	1 (<1)
Cough	26 (20)	0
CRS†	107 (84)	7 (5)

- Cytopenias were common; not dose related
- Median time to recovery of grade ≥3 neutropenia and thrombocytopenia was 2 mo (95% CI, 1.9–2.1) and 3 mo (95% CI, 2.1–5.5), respectively
- Delayed recovery (>1 mo) of grade ≥3 neutropenia in 41% of patients and thrombocytopenia in 48%‡
- Infections (including bacterial, viral, fungal) were common (69%); not dose-related
- 5 deaths (4%) within 8 wk of ide-cel infusion
  - 2 following MM progression
  - 3 from AEs (CRS, aspergillus pneumonia, GI hemorrhage)
- 1 additional death from AE (CMV pneumonia) within 6 mo, in the absence of MM progression

Data cutoff: 14 Jan 2020. AE, adverse event; CMV, cytomegalovirus; CRS, cytokine release syndrome; GI, gastrointestinal.
*Events reported in 20% or more patients. †Clustered term including the preferred term; uniformly graded per Lee DW, et al. ‡Includes 2 patient with grade 5 CRS event was observed.
§Includes patients with grade 3/4 cytopenia at 1 mo post-infusion.

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Reference: Munshi, NC, Anderson LD, Shah N, et al. NEJM.2021; 384:706-716

Presented By Nikhil Munshi at TBD

Toxicities: Infection

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	Number of Infection Events (n=47)		Number of Patients (n=55)	
Severity of Infection	**Any Severity[1]**	**High Severity[2]**	**Any Severity[1]**	**High Severity[2]**
Any infection, n (%)	47 (100)	4 (9)	29 (53)	3 (6)
Bacterial infections, n (%)	19 (40)	3 (6)	15 (27)	3 (6)
Bacterial Site[3], n (%)	14 (30)	2	12 (22)	2 (4)
Gram positive Bacteremia, n (%)	2 (4)	0 (0)	2 (4)	0 (0)
Gram negative Bacteremia, n (%)	3 (6)	1 (2)	3 (6)	2 (4)
Viral Infections, n (%)	25 (53)	0 (0)	18 (33)	2 (4)
Respiratory Virus, n (%)	25 (53)	0 (0)	18 (33)	2 (4)
Other, n (%)	0 (0)	0 (0)	0 (0)	0 (0)
Fungal Infection, n (%)	3 (6)	1 (2)	3 (6)	1 (2)
Mold fungal, n (%)	2 (4)	1 (2)	2 (4)	1 (2)
Non-mold fungal, n (%)	1 (2)	0 (0)	1 (2)	0 (0)
Organ System				
Lower respiratory, n (%)	16 (34)	0 (0)	14 (30)	2 (4)
Upper respiratory, n (%)	16 (34)	0 (0)	14 (30)	2 (4)
Bloodstream, n (%)	1 (2)	1 (2)	1 (2)	1 (2)
GI, n (%)	0 (0)	0 (0)	0 (0)	0 (0)
CNS, n (%)	0 (0)	0 (0)	0 (0)	0 (0)
Other[4], n (%)	14 (30)	3 (6)	9 (16)	2 (4)

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Reference: Kambhampati, S, Sheng, Y, Huang CY, et al. Blood Adv. 2021; Online ahead of print. Doi:10.1182/bloodadvances. 2020004079

COVID 19 deaths

INFECTIOUS MEDICINE, VIROLOGY

Poor outcome of patients with COVID-19 after CAR T-cell therapy for B-cell malignancies: results of a multicenter study on behalf of the European Society for Blood and Marrow Transplantation (EBMT) Infectious Diseases Working Party and the European Hematology Association (EHA) Lymphoma Group

Reference: Spanjaart AM, Ljungman, P, Camara RD et al. Leukemia. 2021; 35: 3585-3588

Toxicities: Infection

Treatment-Emergent AEs	≥40 mg ESC + EXP (n = 75)	All Patients (N = 118[a])
Leading to study drug discontinuation	3 (4)	7 (6)
Leading to study drug interruption[b]	21 (28)	31 (26)
Leading to dose reduction	6 (8)	6 (5)
Associated with DLT	4 (5)	4 (3)
AEs leading to death	3 (4)	6 (5)

Treatment-emergent AE that occurs or worsens on or after the first dose of ABBV-383 until 90 days following discontinuation of study drug administration have elapsed, or until patient starts another anticancer therapy, whichever occurs earlier.

- TEAEs associated with DLTs included
  - Dose escalation, n = 3: platelet count decreased (Gr 4; 60 mg), CRS (Gr 3; 90 mg and 120 mg)
  - Dose expansion, n = 1: CRS (Gr 3; 60 mg)
- Six deaths from TEAEs included
  - COVID-19 (n = 3; 0.025 mg, 0.2 mg, and 60 mg), disease progression (n = 1; 60 mg), liver injury (n = 1; 50 mg), and sepsis (n = 1; 5.4 mg)
- All deaths were considered unrelated to study drug per investigator's assessment

Data cutoff date: Aug 9, 2021.

[a]Safety population defined as patients who have received at least 1 dose of ABBV-383. [b]Includes dose hold or delay.
AE, adverse event; CRS, cytokine release syndrome; DLT, dose-limiting toxicity; ESC, dose escalation; EXP, dose expansion; Gr, grade; TEAE, treatment-emergent adverse event.

Kumar, S, D'Souza A, Shahm, N et al. ASH 2021 abstract #900

COVID antibody response

- Mount Sinai study – suboptimal immune response to mRNA vaccination (2 doses) is associated with BCMA targeted treatment
- UCSF looking at antibody response, data not published yet
- Vaccinations
- Tixagevimab/cilgavimab (Evusheld)

Reference: Oekelen, OV, Agte, S, Aleman, A et al. ASH 2021, abstract #822

Transition to Local Oncologist

- CARs: After first 30 days, generally come to UCSF monthly for first 6 months
- BiTES: We see frequently; may get IVIG or growth factor locally
- Local oncologist to contact us if any complications

Transition to Local Oncologist

- Disease assessment: Monthly labs for myeloma; Lymphoma PET/CT
- IVIG; bone support medications
- Growth factor and transfusion support
- Age appropriate cancer screening

Financial Support

- Research: Trial dependent
- Research: Impact application for assistance – Lazarex Cancer Foundation
- Standard of Care: Financial support program
- Leukemia and Lymphoma Society

Financial Support

- Housing – KOZ house (as an example) vs apartment
- Social worker assistance

Thank you!