# Evaluating PROs in Patients Undergoing CAR-T Cell Therapy

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# Disclosures and Funding

**Disclosures:**

1. Janssen, Advisory Board

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1. ASCO/Conquer Cancer Foundation
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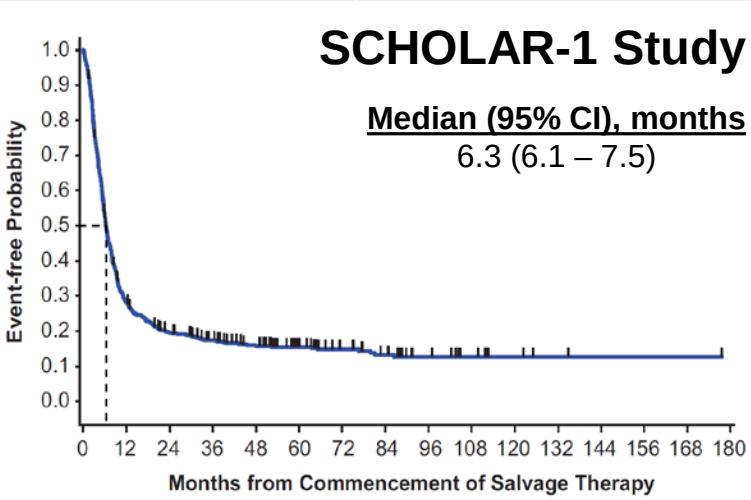
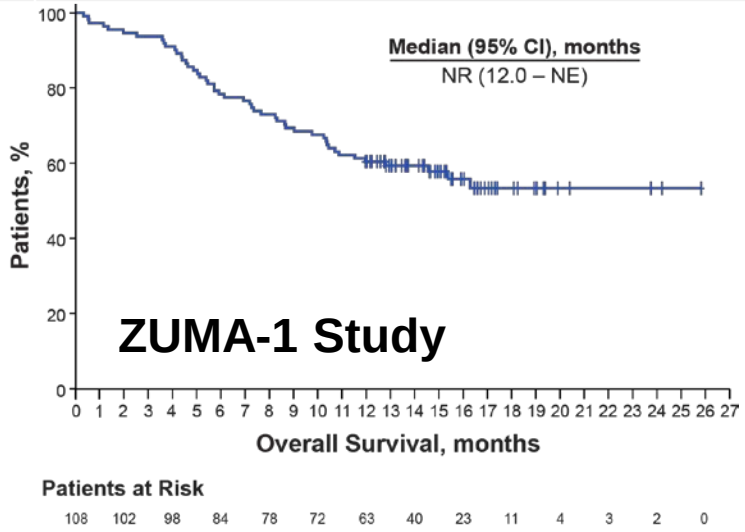
3. Amyloidosis Foundation
4. Mayo Clinic Kern Center for Health Care Delivery

# OS of Salvage Treatments vs Yescarta

| | SCHOLAR-1 | ZUMA-1 |
|---|---|---|
| **Enrollment** | 636 patient from CCTG, CORAL study, MDACC & Iowa/Mayo Lymphoma SPORE | 111 enrolled; 101 dosed |
| **Population** | • 78% refractory<br>• 22% post ASCT<br>• 4% TFL, 2% PMBCL | • 78% refractory; 0% relapsed<br>• 22% post ASCT<br>• 16% TFL; 8% PMCBL |
| **Efficacy** | • **ORR: 26%; 7% CR** | • **ORR: 82%; 54% CR**<br>• Ongoing 6 mo: 44%; 39% CR<br>• Median follow-up 12 m |
| **Safety** | | • G3+ CRS 13%, G3+ NE 28%, G5 AE 3% |




*ZUMA-1: Phase 2 Primary Analysis ASH 2017; Neelapu NEJM 2017.*
*SCHOLAR-1: Crump et al Blood 2017; 130: 1800.*

# Toxicity with CAR-T Cell Therapy


**Unknowns:**

- Long term outcomes
- QOL
- Patient reported symptom burden
- Impact of serious AEs on long term outcomes, PROs

# Approaches to Evaluate PROs: CAR-T

QOL
PROMIS, FACT, SF-36, Others

AEs
NCI PRO CTCAE

Other aspects

Frequency

Duration

Disease specific

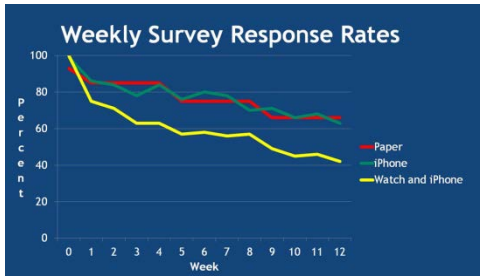
Intervention

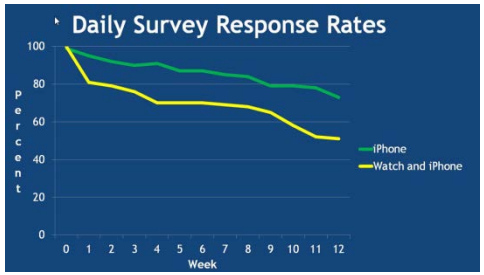


# Approaches: Recent Mayo Hematology Studies

*PRO and Apple watch study*
*C. Thompson et al, ASCO 2018*



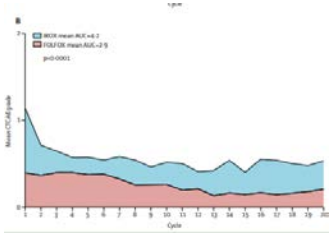


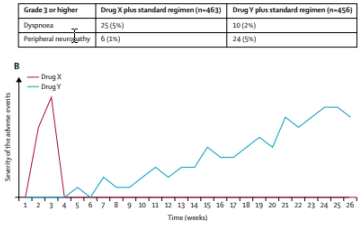
*PROs in patients undergoing CAR-T cell therapy and transplant (QOL, PRO-CTCAE, cognitive side effects) Sidana et al. Ongoing*

The Lancet Haematology Commission

**Beyond maximum grade: modernising the assessment and reporting of adverse events in haematological malignancies**

*Gita Thanarajasingam, Lori M Minasian, Frederic Baron, Franco Cavalli, R Angelo De Claro, Amylou C Dueck, Tarec C El-Galaly, Neil Everest, Jan Geissler, Christian Gisselbrecht, John Gribben, Mary Horowitz, S Percy Ivy, Caron A Jacobson, Armand Keating, Paul G Kluetz, Aviva Krauss, Yok Lam Kwong, Richard F Little, Francois-Xavier Mahon, Matthew J Matasar, María-Victoria Mateos, Kristen McCullough, Robert S Miller, Mohamad Mohty, Philippe Moreau, Lindsay M Morton, Sumimasa Nagai, Simon Rule, Jeff Sloan, Pieter Sonneveld, Carrie A Thompson, Kyriaki Tzogani, Flora E van Leeuwen, Galina Velikova, Diego Villa, John R Wingard, Sophie Wintrich, John F Seymour, Thomas M Habermann*



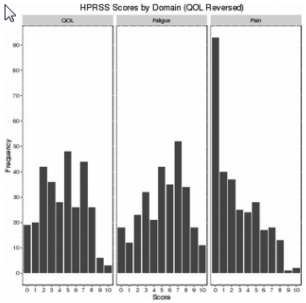



RESEARCH ARTICLE

WILEY AJH

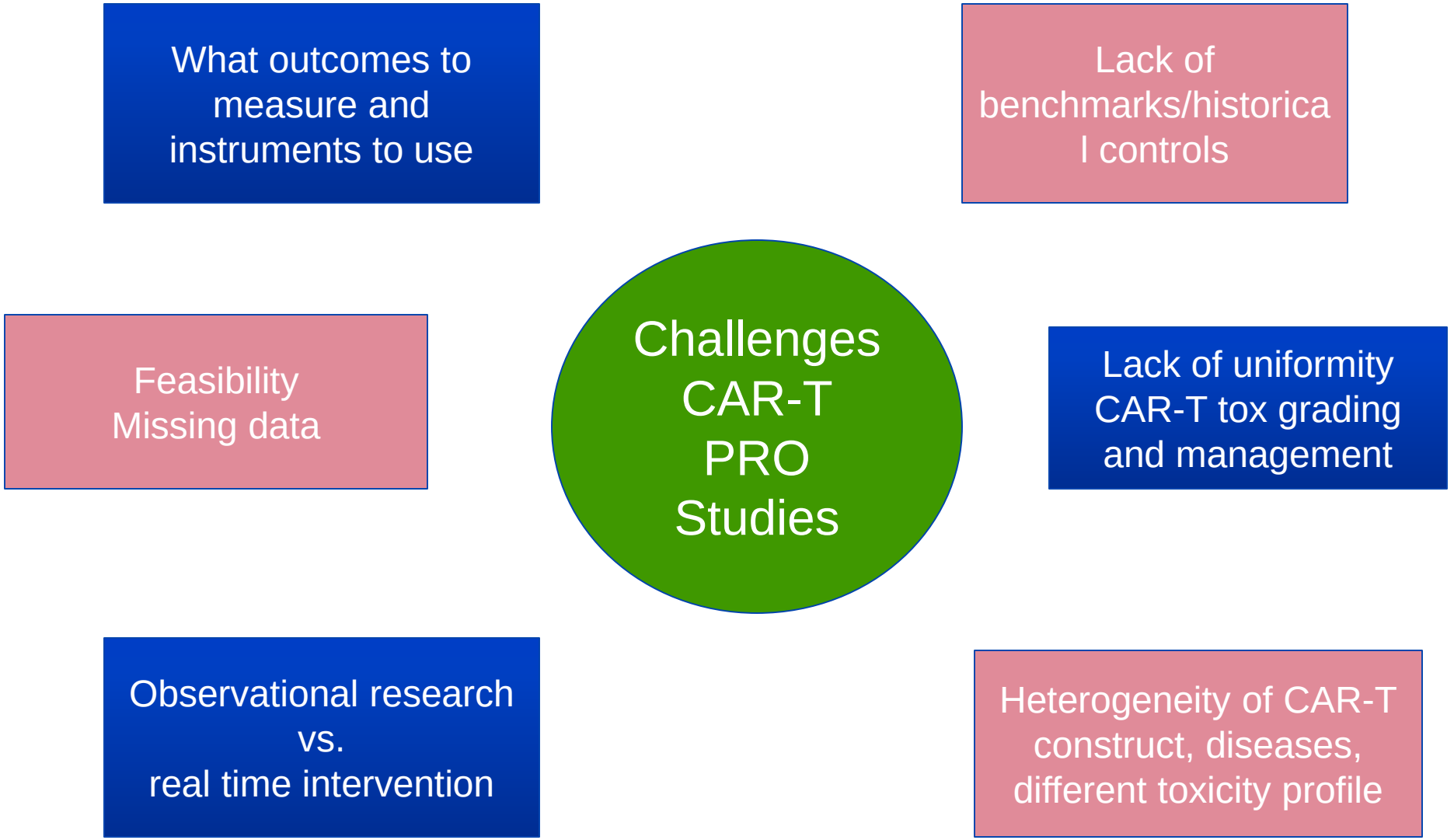
**Hematology patient reported symptom screen to assess quality of life for AL amyloidosis**

Rahma Warsame[1] | Shaji K. Kumar[1] | Morie A. Gertz[1] | Martha Q. Lacy[1] |




*PROs in patients on clinical trials Sidana et al. Ongoing*


What outcomes to measure and instruments to use
Lack of benchmarks/historical controls
Challenges CAR-T PRO Studies
Feasibility Missing data
Lack of uniformity CAR-T tox grading and management
Observational research vs. real time intervention
Heterogeneity of CAR-T construct, diseases, different toxicity profile

# Conducting a PRO study in CAR-T Population: *Issues and Challenges*

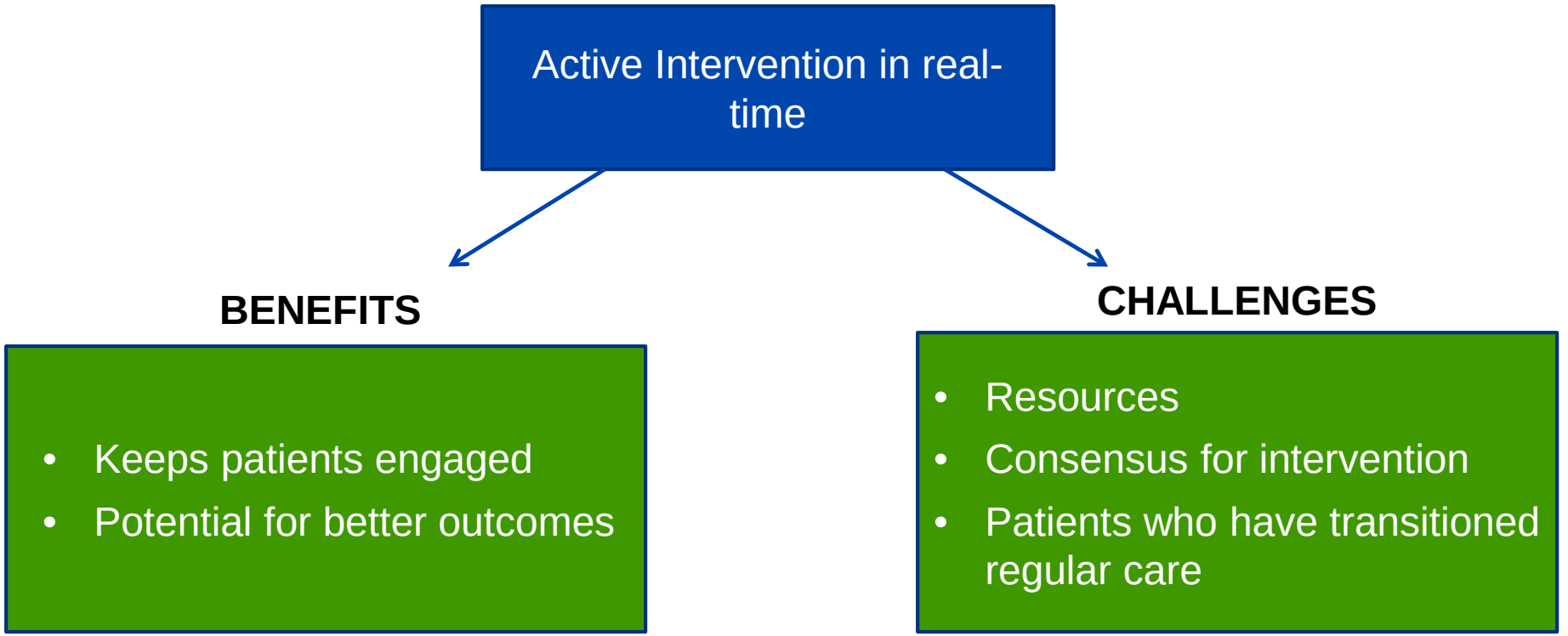
1. Selecting optimal outcomes and instruments for assessing PROs
   - No validated instrument in this population
   - Frequency and duration of assessment
   - Long term issues to address: unknown

2. Feasibility and accounting for missing data
   - Serious AEs: barrier in the short-term, potential for bias
   - Transition of care away from referral centers after CAR-T

# Conducting a PRO study in CAR-T Population: Issues and Challenges

## 3. Observational research vs. active real-time intervention





# Conducting a PRO study in CAR-T Population: *Issues and Challenges*

## 4. Lack of uniformity in grading and management of toxicities

- Toxicity grading and management has varied across different trials
- Each institution has own guidelines for commercially available CAR-T
- CAR-T community still in the process of developing uniform criteria/ guidelines for grading/management of toxicities
- Impact: PRO data collection and interpretation

# Conducting a PRO study in CAR-T Population: *Issues and Challenges*

## 5. Heterogeneity of the CAR-T construct, underlying disease

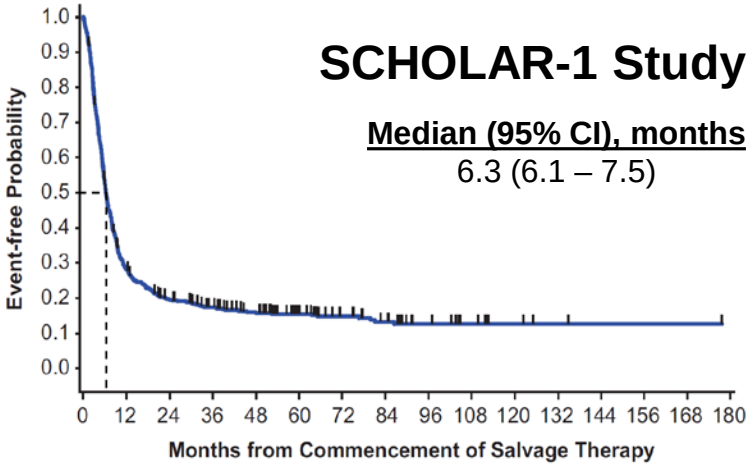
- Current FDA indications: Relapsed DLBCL, ALL in young adults
- Treatment indications may expand in near future (e.g. myeloma)
- Short-term toxicity may vary by CAR-T construct/disease type
- Subsequent therapy for these diseases will vary, impacting PROs
- Disease specific questions would also need to be addressed

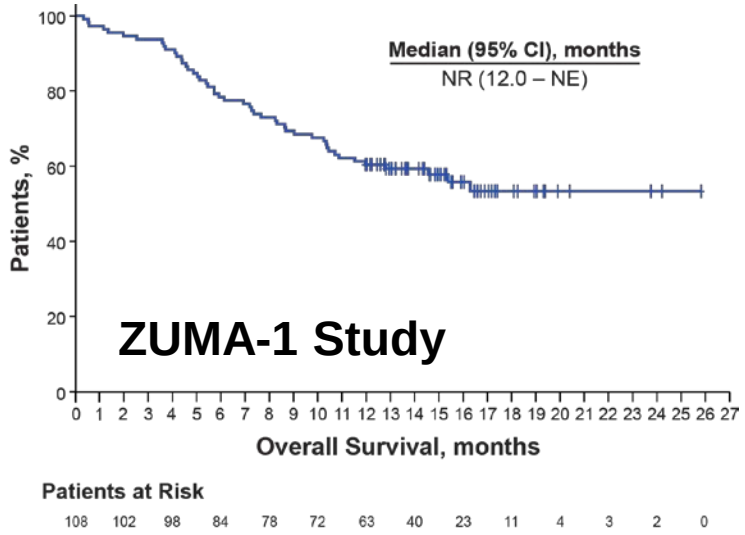

 

# Conducting a PRO study in CAR-T Population: *Issues and Challenges*

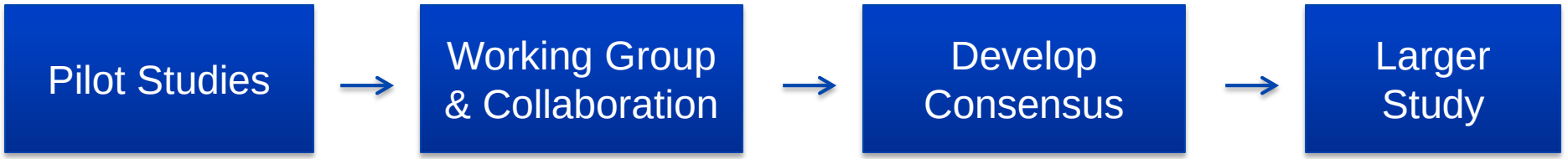
## 6. Lack of benchmarks/historical controls

- Historically, most patients who are currently eligible for CAR-T did not have many cancer-directed treatment options
- What is reasonable QOL in these patients?



# Conducting a PRO study in CAR-T Population: *The Path Forward*




- Feasibility
- Prelim data
- Test different measures
- Need for specific measures

- Outcomes
- Measures
- Implementation strategy

Timeline ~ 12 months

Large scale study in absence of prelim data maybe premature at present