P-020

Treatment Positioning Model to Evaluate the Survival Benefit of Ciltacabtagene Autoleucel in Second-Line Compared With Later-Line Treatment of Lenalidomide-Refractory Multiple Myeloma

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Key Takeaway

Our simulation model suggests that using cilta-cel earlier in the disease course, as early as 2L, may result in better survival than using it for later LOT

Conclusions

Our simulation model estimated a longer survival benefit when using cilta-cel in 2L as opposed to using cilta-cel in 3L+

Models testing alternative distribution models as well as alternative attrition rates suggested longer OS with cilta-cel in 2L as opposed to using cilta-cel in 3L+

Continued investigation with additional real-world data is needed to further evaluate this model

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Poster

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Disclosures

RF is a consultant for AbbVie, Adaptive, Amgen, Apple, BMS/Celgene, GSK, Janssen, Karyopharm, Pfizer, RA Capitol, Regeneron, and Sanofi; is a member of the Scientific Advisory Board for Caris Life Sciences; is a member of the Board of Directors of Antengene; and holds a patent for FISH in MM.

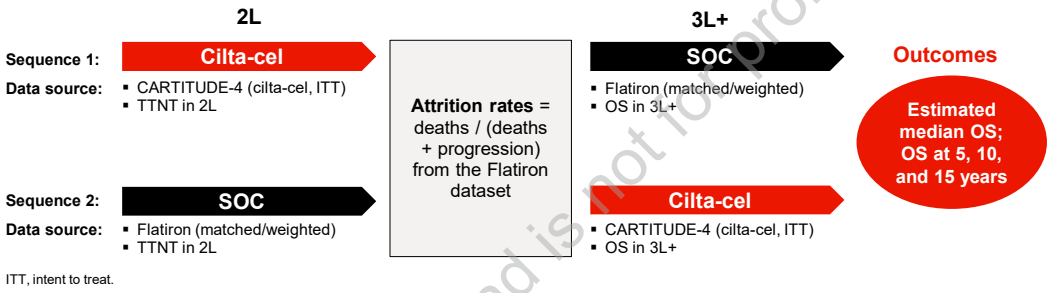
Introduction

- Patients with lenalidomide-refractory multiple myeloma (MM) with 1–3 prior lines of therapy (LOT) have poor outcomes[1,2]
  - Earlier use of chimeric antigen receptor (CAR)-T cell therapies in these patients could lead to improved treatment responses, fewer patients lost to attrition,[3,4] and improved long-term outcomes
- The CARTITUDE-4 study (NCT04181827) evaluated ciltacabtagene autoleucel (cilta-cel) vs physicians' choice of daratumumab, pomalidomide, and dexamethasone or pomalidomide, bortezomib, and dexamethasone, in patients with lenalidomide-refractory MM after 1–3 prior LOT[5]
  - At 15.9-month median follow-up, cilta-cel vs standard of care (SOC) improved progression-free survival (hazard ratio, 0.26 [protocol-specified weighted analysis] and 0.40 [protocol-specified unweighted analysis], both $P<0.001$)
  - Overall survival (OS) data were immature at the time of data cut
- A modeling approach was adapted to evaluate the survival benefit of using cilta-cel vs SOC, from CARTITUDE-4 and the Flatiron Health MM database, earlier in the treatment pathway in patients with relapsed, lenalidomide-refractory MM

Methods

- A Markov model was used to compare the survival benefit of using cilta-cel in second-line (2L) followed by SOC in third-line (3L) or more vs 2L SOC followed by 3L+ cilta-cel
  - SOC therapies used may differ in 2L vs 3L+
- CARTITUDE-4 and the Flatiron Health MM database were used for the efficacy of cilta-cel and SOC, respectively (**Figure 1**)
  - The Flatiron Health MM database provides real-world data from de-identified patients and is a resource for evaluating various SOC therapies[6]
  - 2L cilta-cel was defined as CARTITUDE-4 patients who received 1 prior LOT; 3L+ cilta-cel patients received 2–3 prior LOT
  - SOC was defined based on treatment regimens received by patients with lenalidomide-refractory MM previously treated in 2L and 3L+, with different distributions of treatments between 2L and 3L+
  - Inclusion/exclusion criteria of the CARTITUDE-4 population were applied to the SOC population from the Flatiron cohort and weighted on key prognostic factors and treatment effect modifiers
- Time spent in 2L was defined by time to next treatment (TTNT) and attrition rate in patients on 2L; time spent in 3L+ was defined by OS in patients on 3L+
- Standard parametric survival models were used to estimate the transition probabilities over time
- Attrition rates were assumed to be the same in both arms[7]

Figure 1: Treatment positioning model subgroup data overview



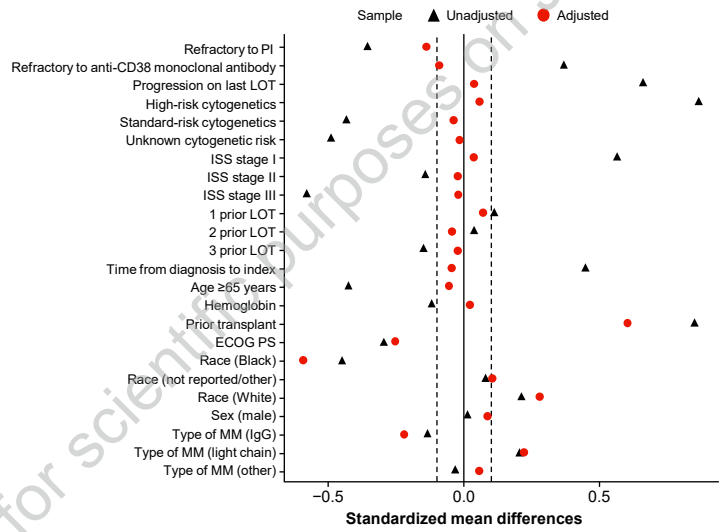
ITT, intent to treat.

Results

Databases

- The cilta-cel arm of CARTITUDE-4 consisted of 208 patients (median follow-up, 15.9 months [range, 0.1–27.3])
- The adjusted Flatiron cohort consisted of 1977 observations (data from February 2016–December 2022; median follow-up, 33.8 months [range, 31.7–36.1])
- In this simulation model, key prognostic factors and treatment effect modifiers from CARTITUDE-4 (cilta-cel) and Flatiron (SOC) subgroups were matched and weighted (**Figure 2**)

Figure 2: Flatiron population matched to CARTITUDE-4 population



ECOG PS, Eastern Cooperative Oncology Group performance status; IgG, immunoglobulin G; ISS, International Staging System; PI, proteasome inhibitor.

- The base case settings used in the model are detailed in **Table 1**

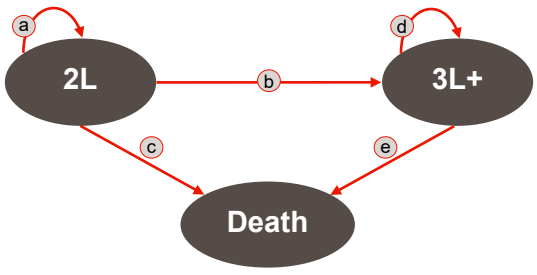
Table 1: Base case settings

Patient characteristics	
Starting age, years	60.1
Female, %	42.7
Survival extrapolation	
General population mortality adjustment	Yes
Flatiron population adjustment	Adjusted (as per **Figure 2**)
Attrition rate, %	**17.1 (applied to both arms)**

Modeling

- A Markov model, including 2L, 3L+, and death was used (**Figure 3**)

Figure 3: Markov model

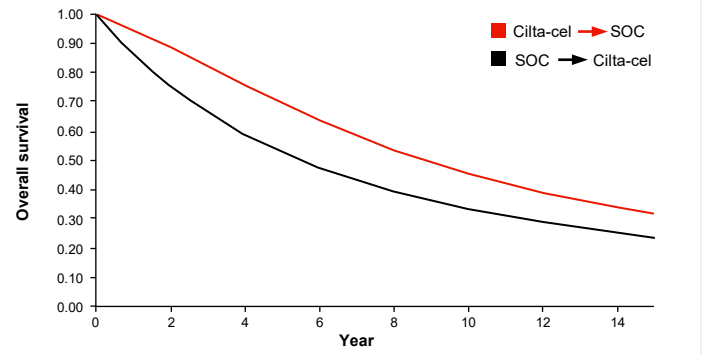


a, % patients who stay on 2L treatment, derived from 2L TTNT; b, % patients who are newly progressed, derived from 2L TTNT and attrition rate; c, % death during 2L treatment, derived from 2L TTNT and attrition rate; d, % patients who stay on 3L+ treatment, derived from 2L TTNT and 3L OS; e, % death during 3L+ treatment, derived from 2L TTNT and 3L OS.

- According to this simulation model, using cilta-cel in 2L resulted in longer OS benefit compared with using cilta-cel in 3L+ after SOC (8.8 vs 5.5 years, respectively; **Figure 4**)

Figure 4: OS (base case)

	2L cilta-cel → 3L+ SOC	2L SOC → 3L+ cilta-cel	Difference
Median OS, years	8.83	5.50	3.33
5 year	69.6%	53.0%	16.6%
10 year	45.6%	33.6%	12.0%
15 year	31.9%	24.0%	7.9%



- Alternative long-term efficacy assumptions were tested using different distribution models for parametric extrapolations (**Table 2**)
  - The predicted OS was longer when using cilta-cel in 2L compared to 3L+ after SOC (8.2 vs 5.4 years, respectively)
- Alternative attrition rates (44.6%) were also tested, which included censored patients (**Table 2**)
  - The predicted OS was longer when using cilta-cel in 2L compared to using cilta-cel in 3L+ after SOC (7.4 vs 3.0 years, respectively)
- Alternative scenario analyses (data not shown) consistently demonstrated the survival benefit of using cilta-cel earlier vs later

Table 2: OS (alternative distribution and attrition rates)

		2L cilta-cel → 3L+ SOC	2L SOC → 3L+ cilta-cel	Difference
Alternative distribution model	Median OS, years	8.17	5.42	2.75
	5 year	68.2%	52.6%	15.6%
	10 year	42.1%	33.8%	8.2%
	15 year	27.6%	24.5%	3.1%
Alternative attrition rates	Median OS, years	7.42	3.00	4.42
	5 year	61.9%	38.2%	23.6%
	10 year	41.0%	23.4%	17.6%
	15 year	29.4%	16.5%	12.8%

Limitations

- Attrition rates in CAR-T patients are unknown, therefore the model assumed the same attrition rate as with SOC
- Utilizing a combination of data sources from clinical trials and real-world evidence poses challenges; however, it is currently the most effective approach available, and the objective of this study was to simulate against SOC
- The prespecified primary analysis of CARTITUDE-4 had a median follow-up of 15.9 months; additional follow-up is required to determine long-term efficacy
- Future validation of our treatment positioning model will be completed with a later CARTITUDE-4 data cut

References

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Multiple Myeloma

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