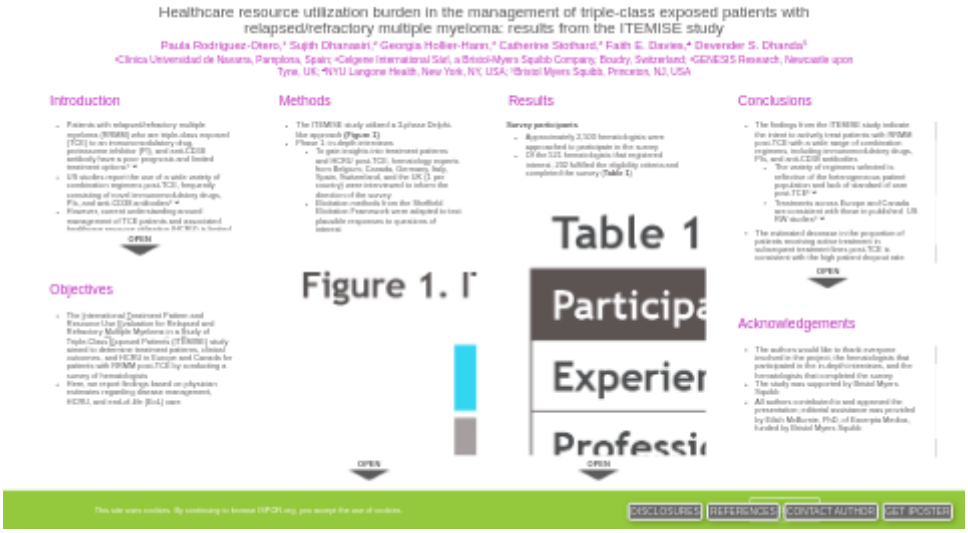
Healthcare resource utilization burden in the management of triple-class exposed patients with relapsed/refractory multiple myeloma: results from the ITEMISE study



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INTRODUCTION

- Patients with relapsed/refractory multiple myeloma (RRMM) who are triple-class exposed (TCE) to an immunomodulatory drug, proteasome inhibitor (PI), and anti-CD38 antibody have a poor prognosis and limited treatment options[1–4]
- US studies report the use of a wide variety of combination regimens post-TCE, frequently consisting of novel immunomodulatory drugs, PIs, and anti-CD38 antibodies[1–4]
- However, current understanding around management of TCE patients and associated healthcare resource utilization (HCRU) is limited outside the US[5]
- Despite the use of novel agents, current treatments post-TCE are associated with poor prognosis and short treatment duration, due to disease progression[1–4]
  - In a real-world (RW) patient cohort, the KarMMa-RW study[3] reported a median progression-free survival (PFS) of 3.5 months (95% confidence interval [CI] 3.2–3.7) and median overall survival (OS) of 14.7 months (95% CI 14.0–15.4) for patients in their first treatment post-TCE
  - An IBM MarketScan study by Madduri et al.[4] reported a median time to treatment discontinuation of 4.2 months (95% CI 3.1–5.2) and time to next treatment of 6.2 months (95% CI 5.4–8.0) for first treatment post-TCE
- Patient management post-TCE incurs high HCRU and costs
  - Madduri et al.[4] reported a mean all-cause total cost in US dollars (USD) of 37,033 per patient per month, with multiple myeloma (MM) treatment accounting for 96% of costs

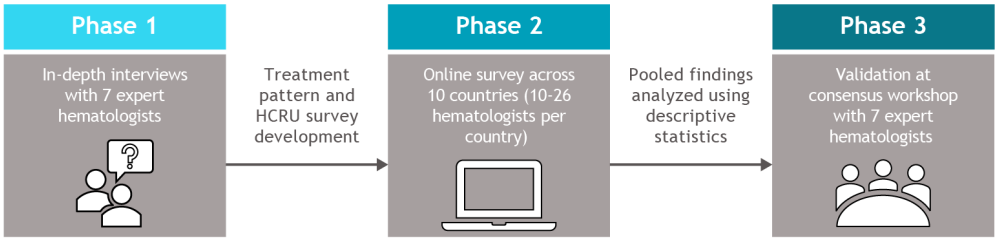
OBJECTIVES

- The International Treatment Pattern and Resource Use Evaluation for Relapsed and Refractory Multiple Myeloma in a Study of Triple-Class Exposed Patients (ITEMISE) study aimed to determine treatment patterns, clinical outcomes, and HCRU in Europe and Canada for patients with RRMM post-TCE by conducting a survey of hematologists
- Here, we report findings based on physician estimates regarding disease management, HCRU, and end-of-life (EoL) care

METHODS

- The ITEMISE study utilized a 3-phase Delphi-like approach **(Figure 1)**
- Phase 1: in-depth interviews
  - To gain insights into treatment patterns and HCRU post-TCE, hematology experts from Belgium, Canada, Germany, Italy, Spain, Switzerland, and the UK (1 per country) were interviewed to inform the direction of the survey
  - Elicitation methods from the Sheffield Elicitation Framework were adapted to test plausible responses to questions of interest

Figure 1. ITEMISE study design



HCRU, healthcare resource utilization; ITEMISE, International Treatment Pattern and Resource Use Evaluation for Relapsed and Refractory Multiple Myeloma in a Study of Triple-Class Exposed Patients.

- Phase 2: development of a cross-sectional survey
  - The survey was fielded to hematologists across Belgium, Canada, France, Germany, Italy, the Netherlands, Spain, Sweden, Switzerland, and the UK from August to October 2020
  - Hematologists with ≥ 3 years experience post-medical training, who spend > 50% of their professional time on direct patient care, and treat ≥ 5 patients with RMMM post-TCE in a typical year were eligible
  - Pooled survey findings for all countries were analyzed using descriptive statistics including measures of central tendency and spread
- Phase 3: final consensus workshop with phase 1 hematology expert leaders
  - Aimed to discuss and validate pooled findings according to clinical practice in Europe and Canada and compare with US RW data

Population of interest

- Hematologists were asked to consider TCE patients with RRMM
  - A high proportion of patients were expected to be refractory to previous treatments, be of a relatively young age (median age of 65 years), and have a good performance status (Eastern Cooperative Oncology Group performance status 0–1)

RESULTS

Survey participants

- Approximately 2,500 hematologists were approached to participate in the survey
- Of the 521 hematologists that registered interest, 202 fulfilled the eligibility criteria and completed the survey (**Table 1**)

Table 1. Characteristics of hematologist survey participants

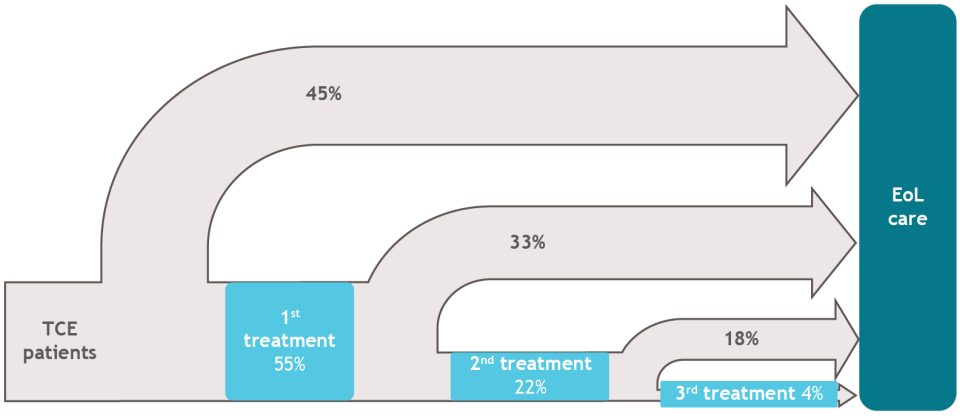
Participant characteristic	N = 202
Experience post-training, median (IQR), years	17 (12-22)
Professional time spent on patient care, median (IQR), %	85 (80-95)
Institution type, n (%)	
Academic/tertiary hospital	121 (60)
Public hospital	76 (38)
Private hospital	5 (2)
Number of MM patients treated per year, median (IQR)	65 (40-100)
Number of RRMM patients treated per year, median (IQR)	34 (25-60)
Number of RRMM patients post-TCE treated per year, median (IQR)	15 (10-35)

IQR, interquartile range; MM, multiple myeloma; RRMM, relapsed/refractory multiple myeloma; TCE, triple-class exposed.

Patients receiving treatment post-TCE

- In the survey, hematologists estimated that 55% (interquartile range [IQR] 30–75) of patients received active treatment post-TCE and the remaining 45% of patients proceed to EoL care (**Figure 2**)
- The percentage of patients estimated to receive active treatment decreased through subsequent treatment lines

Figure 2. Proportion of patients estimated to have received active treatment post-TCE



Percentages represent the proportion of patients following each route post-TCE.
EoL, end of life; TCE, triple-class exposure.

First active treatment post-TCE

- Hematologists selected up to 5 regimens and estimated the percentage of patients that would receive each regimen for first treatment post-TCE
  - A total of 166 unique regimens were selected
    - 87% of patients were estimated to receive a regimen containing either an immunomodulatory drug, PI, or anti-CD38 antibody for first treatment post-TCE

- Regimens containing an immunomodulatory drug (alone or ± an alternative drug class ± chemotherapy ± steroid agent) were most frequently used, received by an estimated 22.5% of patients (groupings mutually exclusive) (**Table 2**)

- Pomalidomide, daratumumab, and lenalidomide were the most frequently selected MM drugs (excluding dexamethasone), received by an estimated 33%, 26%, and 25% of patients, respectively

- Following consensus validation, hematology experts agreed that immunomodulatory drug- and PI-based regimens are used most frequently post-TCE and treatment duration was estimated at 4–6 months

Table 2. Drug class combinations used for first active treatments post-TCE

Drug class combination	Mean proportion of patients estimated to receive regimen (%)
Immunomodulatory drug[a]	22.5
Anti-CD38 antibody and immunomodulatory drug[a]	17.8
PI[a]	15.1
Immunomodulatory drug and PI[a]	13.2
Chemotherapy and/or steroid	8.1
Anti-CD38 antibody and IMiD and PI[a]	7.1
Anti-CD38 antibody[a]	6.2
Anti-CD38 antibody and PI[a]	5.1
Alternative drug classes (± chemotherapy ± steroid)	4.9

Groupings are mutually exclusive.
[a]± Alternative drug class (elotuzumab, panobinostat, venetoclax, or nelfinavir) ± chemotherapy ± steroid.
PI, proteasome inhibitor; TCE, triple-class exposure.

HCRU post-TCE: outpatient visits

- Outpatient visits (defined as a hospital consultation with a healthcare practitioner) are required prior to and during treatment, for example for health monitoring tests or scans
- Hematologists surveyed estimated that patients require 2 outpatient visits prior to initiating a new treatment line (**Table 3**) estimated to be 1 hour (IQR < 1–2) in duration (excluding patient waiting time)
- During active treatment post-TCE, hematologists estimated that patients require 2 outpatient visits per month (excluding visits for MM drug administration) (**Table 3**)
  - Approximately 90% (IQR 50–100) of patients would see a hematologist for an average of 30 minutes (IQR 20–30) per visit
- Hematology experts agreed that the survey estimates reflect clinical practice, but considered that the number of visits could be subject to differences between countries and national guidelines

Table 3. Estimated number of outpatient visits for TCE patients

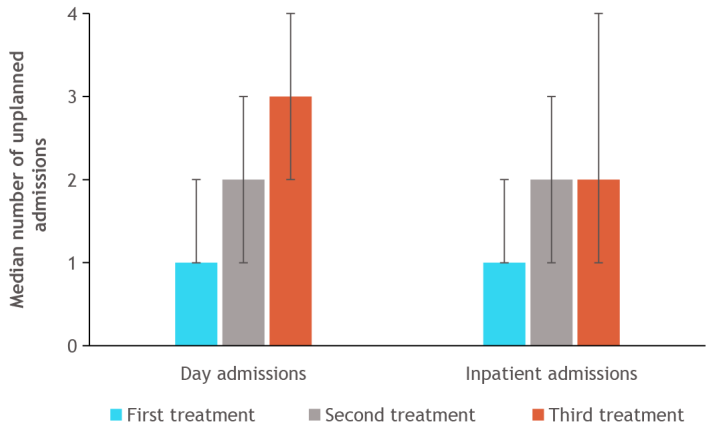
Estimated number of outpatient visits, median (IQR)		Total estimated number of outpatient visits by number of treatments post-TCE, median[a]		
Prior to initiating a treatment line	Per month of active treatment	1 active treatment	2 active treatments	3 active treatments
2 (2-3)	2 (1-3)	12	20	26

[a]Calculated assuming 2 visits prior to each treatment line, 2 visits per month during each treatment and a treatment duration of 5, 3, and 2 months for first, second, and third treatment post-TCE, respectively, according to ITEMISE consensus validation estimates.
IQR, interquartile range; ITEMISE, International Treatment Pattern and Resource Use Evaluation for Relapsed and Refractory Multiple Myeloma in a Study of Triple-Class Exposed Patients; TCE, triple-class exposed.

HCRU post-TCE: unplanned hospitalizations

- Hematologists estimated that patients would have 2 unplanned hospitalizations (1 day admission and 1 inpatient admission, **Figure 3**) during first active treatment post-TCE
- The estimated number of unplanned hospitalizations increased through subsequent treatment lines, with infections considered the main driver
- Hematology experts considered these estimates slightly higher than observed in clinical practice, as institutions would have procedures (such as health monitoring tests and concomitant medication) that aim to pre-empt and reduce the need for hospitalizations

Figure 3. Estimated number of unplanned hospitalizations in each treatment line post-TCE



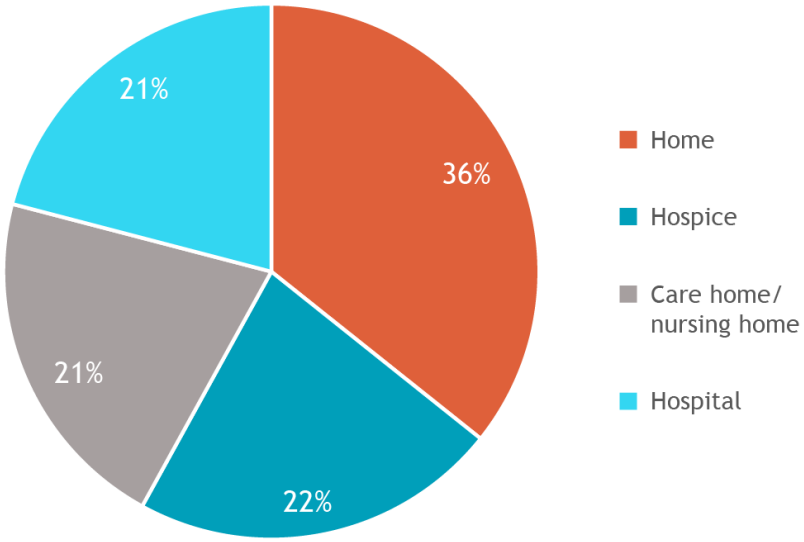
Error bars show IQR. A day admission requires a bed but not an overnight stay. An inpatient admission requires at least 1 overnight stay in the hospital. IQR, interquartile range; TCE, triple-class exposure.

EoL care post-TCE

- Hematologists estimated that patients would spend 3 months (IQR 2–3) in EoL care (defined as supportive care given to patients who are near EoL and have stopped treatment to cure or control their disease) following treatment post-TCE
- Most of those patients (79%) were expected to spend the majority of EoL outside the hospital (**Figure 4**)
  - Of the patients that receive care outside the hospital, 2 outpatient visits (IQR 1–4) would be required during EoL care, e.g. for blood transfusions or pain relief
- It was estimated that patients would have 2 unplanned hospitalizations (IQR 1–3) during EoL care consisting of 6 bed days (IQR 4–10) per admission

- Hematology experts confirmed findings that patients spend 1–3 months in EoL care, depending on patient and clinician preferences

Figure 4. Percentage of TCE patients that spend EoL in each location



EoL, end of life; TCE, triple-class exposure.

CONCLUSIONS

- The findings from the ITEMISE study indicate the intent to actively treat patients with RRMM post-TCE with a wide range of combination regimens, including immunomodulatory drugs, PIs, and anti-CD38 antibodies
  - The variety of regimens selected is reflective of the heterogeneous patient population and lack of standard of care post-TCE[1–4]
  - Treatments across Europe and Canada are consistent with those in published US RW studies[1–4]
- The estimated decrease in the proportion of patients receiving active treatment in subsequent treatment lines post-TCE is consistent with the high patient dropout rate observed in published studies[6,7]
- Unplanned hospitalizations were estimated to increase through subsequent treatment lines, which aligns with observational studies that have reported an increase in toxicities in later treatment lines[7]
  - Anti-myeloma treatments, drug administration, and unplanned hospitalizations are key cost drivers in RRMM[4,8–10]
- The high HCRU burden associated with the management of patients post-TCE highlights the significant need for better treatment options and effective guidelines to reduce this burden across Europe and Canada

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DISCLOSURES

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