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Mapping of Treatment Lines and Regimens for Multiple Myeloma Patients in Sweden

If utilized correctly, Swedish health-care information systems, combined with data from national registries, can provide valuable treatment pattern information and outcomes data

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Aims

To assess the feasibility of utilizing healthcare information systems from five Swedish regions to evaluate how treatment of multiple myeloma varied with line of therapy and time, from 2017 to 2021

Background

- Therapeutic options for treating multiple myeloma (MM) are increasing, imposing a challenge to the treating physician in selecting the optimal treatment strategy
- The Swedish quality registry for myeloma, initiated in 2008, has excellent coverage but limited data on treatment pattern beyond 1L
- The research focused company Reveal, with real-world data generation as one of their specialities, has access to patient data from healthcare information systems from 2015
- Reveal's dataset enables long-term follow-up of myeloma patients, including treatment pattern data from 2L and later

Demographics and data sources

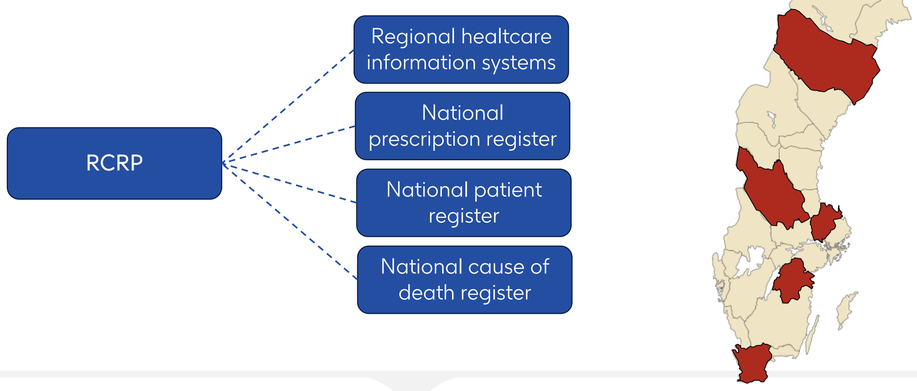
Reveal's Cancer Research Program (RCRP)

RCRP contains a set of data from clinical healthcare information systems and registers, enabling long-term follow-up to provide data on treatment pattern from 2L and beyond. At the time of the assessment, the data covered five Swedish regions (outlined in Fig. 1): Skåne, Västerbotten, Dalarna, Uppsala and Östergötland from 2015-2021.
Data coverage: 27% of the total Swedish population*

Personal identity numbers are used to link regional administration data to national administrative registers from the National Board of Health and Welfare (NBHW)[2] for: 1. prescribed drugs, 2. outpatient/inpatient care records and 3. National cause of death register. See Table S1 for details.

*10,5 million inhabitants per May 2023 (source: SCB[1])

Figure 1: **Data sources and Swedish regions**



Study design

Patient selection criteria

Data was retrieved and processed between November 2022 – March 2023

Eligible patients must have:
- received a multiple myeloma (MM) diagnosis, C90, AND received a cancer drug treatment after the first C90 diagnosis in any of the five regions between 2015-2021

Patients were excluded if they had:
- their first C90 diagnosis appearing before 2017 OR after June 2021
- record of MM treatments outside the five regions, defined as:
  - Prescription of drugs of special interest for multiple myeloma (Systemic Anti-Cancer Therapy [SACT]) outside of the region OR
  - Administration of unspecific cytostatic drugs OR
  - Procedure codes for unspecific drugs outside of the region AFTER, or at the same visit as receiving first C90

Definition of ASCT lines[3,4]

The following rules were set for defining a treatment period an "ASCT line" (outlined in Figure S1):
- Multiple ASCT events occurring within 365 days
- All SACT given within 180 days before the first ASCT event and
- All SACT given within 180 days after the last ASCT event
- SACT treatment that was started within 180 days after the last ASCT (maintenance treatment) will extend the line until a new drug is added or treatment is interrupted for 90 days.

Hence, SACT drugs given within an ASCT-line* were included in the same treatment line.

* Sometimes referred to as Induction, Mobilization, High-dose, Consolidation and Maintenance treatments.

Definition of MM treatment regimens

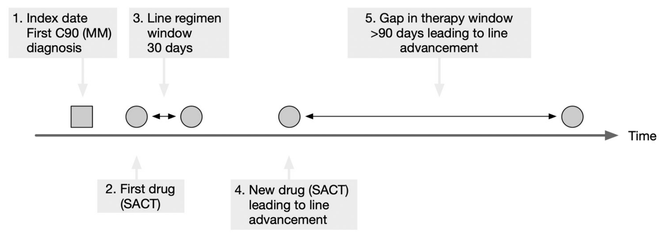
The National treatment guidelines for myeloma[3] were used to define treatment regimens. A typical myeloma treatment regimen combines 2-4 drugs including a corticosteroid (steroid). Additional drugs represent: CD38 antibodies, proteasome inhibitors (PI), immunomodulatory drugs (IMiD), and sometimes chemotherapy (chemo). Nearly 30 regimens were recommended in the guidelines at the time of assessment. Other drug combinations identified in this dataset were labeled "not in guidelines" (Table S2). Table 2 lists drugs included in MM regimens, referred to as SACT.

In addition to drug treatment, patients undergoing Autologous Stem Cell Transplantation (ASCT) were identified using procedure codes.

ATC code	Drug class	Substance	Abbrev	Identifiable in dataset	Brand name
H02	Steroid	dexamethasone	d	No	Decadron
H02	Steroid	prednisolone	p	No	Prednisolone
L01	Chemo	cisplatin	P	Yes	Platinol
L01	Chemo	cyclophosphamide	C	Yes	Sendoxan
L01	Chemo	melphalan	M	Yes	Alkeran
L01	Chemo	Bendamustine	B	Yes	Bendamustine
L01	Chemo	etoposide	E	Yes	Vepesid
L01	Chemo	doxorubicin	A	Yes	Adriamycin
L01	CD38 ab	daratumumab	Dara	Yes	Darzalex
L01	PI	bortezomib	V	Yes	Velcade
L01	PI	carfilzomib	K	Yes	Kyprolis
L01	PI	Ixazomib	I	Yes	Ninlaro
L04	IMiD	thalidomide	T	Yes	Thalidomide
L04	IMiD	lenalidomide	R	Yes	Revlimid
L04	IMiD	pomalidomide	P	Yes	Imnovid

Table 2: **SACT drugs and classes**

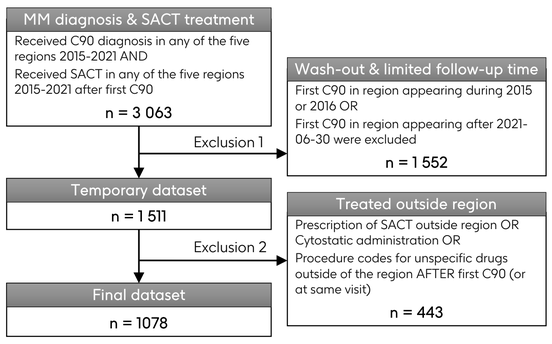
Figure 2: **definition of treatment lines[3,4] – correcting for dose delays, sequential administration of drugs in a regimen, and absence of corticosteroid data**



1. The first registered C90 diagnosis is the index date for treatment line identification.
2. A treatment line is considered initiated when the first drug in a myeloma regimen is administered.
   - the first MM drug given after C90 diagnosis defines the first treatment line.
   - the first MM drug in subsequent treatment lines would define initiation of those.
3. A 'Line regimen window' is set to 30 days, meaning that addition of a 'new MM drug' 0-29 days after drug 1 does not lead to line advancement.
4. Addition of a 'new MM drug' ≥30 days after drug 1 leads to line advancement.
5. Interruption of drug treatment (or 'Gap in therapy window') for longer than 90 days leads to line advancement.
   - line advancement is considered even if the treatment is reinitiated with the same regimen.
   - breaks shorter than 90 days do not lead to line advancements.

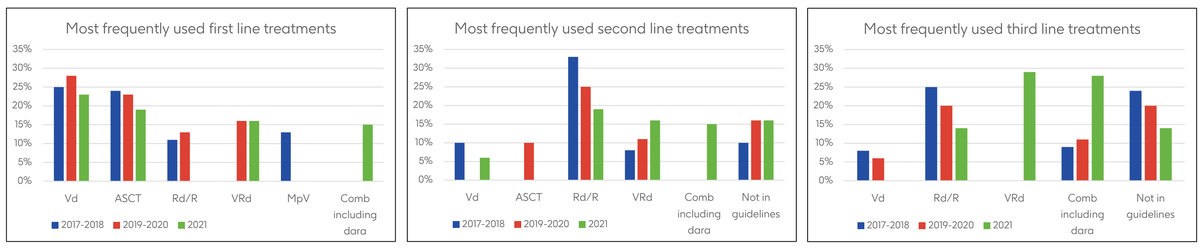
Results

Figure 3: **Patient selection**



- A total of 1,078 patients were included in the final analysis dataset.
- As per inclusion criteria, all patients had at least one treatment line.
- Observed patient distribution over treatment lines 2-5:
  - 51% had received 2 lines,
  - 27% 3 lines,
  - 14% 4 lines and,
  - 7% 5 lines.

Figure 4: **treatment pattern over time**

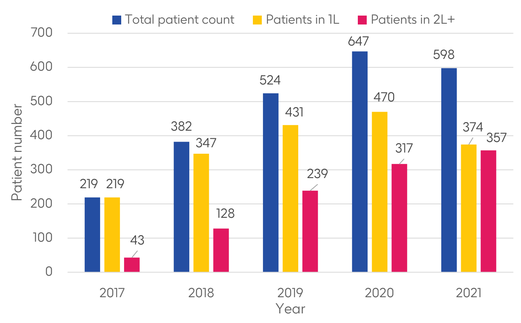


- The percentage of patients receiving ASCT (~30%; n=286/1078), is roughly in line with national quality registry data[7].
- Vd and ASCT are the most common first line treatments regardless of time period.
- Use of lenalidomide remains high throughout treatment lines and time periods, being included in different regimens.
- There is a noticeable use of drug combinations including daratumumab across all lines, being used in ~15% each of both 1L and 2L patients in 2021.
- Pomalidomide containing regimens were not among the most frequently used regimens in 1L-3L within the study time period.*
- Use of drug combinations not included in the guidelines becomes increasingly more prevalent the later the line, starting with ~13% of all patients at second line.

* Figure S2 displays all regimens picked up in this dataset and how frequently they are used in 1L.

Combinations including daratumumab: Dara-d, Dara-Rd, Dara-VCd, Dara-Vd, Dara-VRd, Dara-VTd.
Abbreviations: ASCT=autologous stem cell transplantation; C=cyclophosphamide; d=dexamethasone; Dara=daratumumab; M=melphalan; p=prednisolone; R=lenalidomide; T=thalidomide; V=bortezomib.

Figure 5: **Patients in 1L, 2L+, and in total**



- Patients receiving a first line treatment ranged from 219 to 470 between 2017-2021 (yellow bars). The decrease observed in 2021 is due to exclusion of patients diagnosed after June 2021.
- Patients treated in subsequent lines increased from 43 to 357 between 2017 and 2021 (red bars). Treated patients regardless of treatment line peaked at 647 in 2020 (blue bars).
- 43 of the 219 patients receiving first line treatment advanced to second line or later during the same calendar year. Importantly, a patient can receive one or more new treatment lines in one year, thus the "Total patient count" is lower than the sum of "Patients in 1L" and "Patients in 2L+".

Conclusions

Data from the regions can be a useful source for assessing treatment patterns, beyond first line, over time for Swedish MM patients

By utilizing well defined algorithms for line advancement and ASCT lines, our data was in line with what has previously been published[5,6], thus validating the selection criteria

The changes over time in treatment regimens used reflect the reimbursement pattern in Sweden[8,9], and regimens not in guidelines are common already in second line

Abbreviations

1L=first line; 2L=second line; 3L=third line; ASCT=Autologous Stem Cell Transplantation; ATC=Anatomical Therapeutic Chemical; C=cyclophosphamide; d=dexamethasone; Dara=daratumumab; IMiD=immunomodulatory imide drug; M=melphalan; MM=Multiple Myeloma; NBHW=The National Board of Health and Welfare; p=prednisolone; PI=proteasome inhibitor; R=lenalidomide; RCRP=Reveal's Cancer Research Program; SACT=Systemic Anticancer Therapy; SCB=Statistics Sweden; T=thalidomide; V=bortezomib

References

1. SCB Statistics Sweden: https://www.scb.se/en/; 2. The National Board of Health and Welfare: https://www.government.se/government-agencies/national-board-of-health-and-welfare--socialstyrelsen/; 3. National Treatment Guidelines Myeloma (Swedish): https://kunskapsbanken.cancercentrum.se/diagnoser/myelom/vardprogram/; 4. National clinical expert; 5. Liwing et al., Br J Haematol. 2014.; 6. Yong et al., Br J Haematol. 2016; 7. National Quality Registry for Myeloma (Swedish): https://cancercentrum.se/samverkan/cancerdiagnoser/blod-lymfom-myelom/myelom/kvalitetsregister/; 8. National Joint Introduction process: https://samverkanlakemedel.se/process---ordnat-inforande/national-joint-introduction; 9. The Dental and Pharmaceutical Benefits Agency: https://www.tlv.se/in-english.html.

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Disclosures

AA and JG are employed by GSK and hold financial equities in GSK.
LD was employed by GSK at the time of the study.
KI and KÅ are employed by Reveal and their participation in this study was sponsored by GSK.

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