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SUBCUTANEOUS DARATUMUMAB IN THE TREATMENT OF MULTIPLE MYELOMA IN ITALY: A BUDGET IMPACT ANALYSIS

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Objective

- Daratumumab administered via an intravenous infusion (dara-IV) is currently approved for the treatment of patients with multiple myeloma, both newly diagnosed (NDMM) and relapsed/refractory (RRMM)
- A daratumumab formulation for subcutaneous administration (dara-SC) was developed with the goal of shortening treatment administration without compromising safety and efficacy
- Dara-SC was licensed in 2020 and is expected to be reimbursed in the Italian setting for the same indications as dara-IV
- This analysis assesses the budget impact of switching Italian patients currently receiving dara-IV to dara-SC
- The analysis was conducted over a 3-year horizon from the Italian societal perspective

Table 1. Daratumumab reimbursed indications

NDMM ineligible for ASCT	NDMM eligible for ASCT	RRMM	RRMM ≥3PLs
DVMP	DVTd	DRd	Dara
DRd		DVd	

Table 2. Parametric distributions for TTD

	Parametric distribution	Source/Rationale
NDMM ineligible for ASCT		
DVMP SC	Gompertz	Same as DVMP IV
DVMP IV	Gompertz	MMY3007; median follow-up 40.1 months
DRd SC	Exponential	Same as DRd IV
DRd IV	Exponential	MMY3008; median follow-up 56.2 months
NDMM eligible for ASCT		
DVTd SC	N/A	Same as DVTd IV
DVTd IV	Observed data	MMY3006; median follow-up 18.8 months
RRMM		
DRd SC	Exponential	Same as DRd IV
DRd IV	Exponential	MMY3003 IA3; median follow-up 54.8 months
DVd SC	Gompertz	Same as DVd IV
DVd IV	Gompertz	MMY3004 IA3; median follow-up 50.0 months
RRMM ≥3PLs		
Dara SC	Log-logistic	Same as Dara IV
Dara IV	Log-logistic	MMY2002; median follow-up 37.6 months

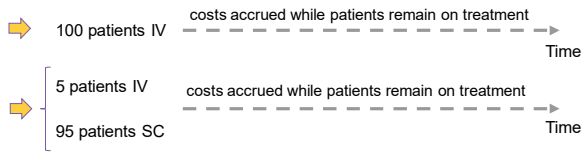
References

1.Darzalex® (daratumumab). Summary of product characteristics **2**.Study MMY3012 (COLUMBA) NCT03277105 **3**.Study MMY2040 (PLEIADES) NCT03412565 **4**.Lazzaro C. Clinicoecon Outcomes Res. 2013 Apr 11;5:125-35 **5**.Mickisch G. Br J Cancer. 2010 Jan 5;102(1):80-6 **6**. Ministero della Salute. GU Serie Generale 23 (28-1-2013) **7**.Franzini JM, Volpe M. Bisogni, evidenze ed evoluzione del sistema. Il caso delle formulazioni sottocutanee. I quaderni di quotidianosanità.it. 2018 **8**.Pradelli L. Farmeconomia. Health economics and therapeutic pathways 2017; 18(1): 5-14 **9**. Cicchetti A. Mini HTA di rituximab e trastuzumab in formulazione sottocutanea, Working Paper Altems n. 1, 2017

Methods

- The analysis included all currently reimbursed indications [1] (Table 1)
- In line with clinical trials results [2,3], we assumed that **dara-SC and dara-IV regimens are equally effective**
- Parametric distributions based on latest time-to-treatment discontinuation (TTD) data from clinical trials (Table 2) were used to estimate the number of patients who remain on treatment over time
- Cost categories included were: i) drug administration ii) treatment of adverse events and iii) productivity loss, because of time required for drug administration
- **Drug acquisition costs were assumed to be equivalent for dara-IV and dara-SC regimens and therefore not considered**
- Unit costs were collected from published literature [4,5] and institutional Italian data [6] (Table 3)
- In a cohort of 100 dara-IV patients per approved regimen, the model simulates the switch to dara-SC of 95% of them (Figure 1)

Figure 1. Model structure



Results

Switching 95% of patients to dara-SC results in a saving of resources for all regimens considered in every cost category. Over 3 years, the greatest savings (€ 1,189,669) were observed for DRd in RRMM patients.

Conclusions

The introduction of dara-SC in Italy for the treatment of patients with multiple myeloma can help save resources.

Table 2. Unit costs

Daratumumab administration (€ per infusion)	
Dara-SC infusion	N/A
Dara-EV infusion	1st and 2nd € 384.76 Subsequent € 242.03
Productivity loss (€ per hour lost)	
50-59 years	€9.92
60-64 years	€ 11.49
≥ 65 years	€ 3.62

Administration

In the SCuBA (SubCutaneous Benefit Analysis) project [7], the costs of trastuzumab and rituximab IV and SC administration were investigated in an incremental way. Rituximab results were used as a proxy to estimate the incremental cost of dara-IV with respect to dara-SC. The estimated savings for rituximab SC were adjusted to account for the different duration of daratumumab administration. Some savings items were assumed independent of the difference in duration between SC and IV administration (i.e. venous accesses, consumables, and drug preparation time), while other items were assumed directly proportional to the difference in duration between SC and EV administration (i.e. nursing staff time for administration and overhead costs). In the analysis, the cost of dara-SC infusion is assumed to be zero and the cost of dara-IV infusion is equal to the estimated savings. The cost of administering other drugs is not considered as it is not differential when comparing regimens involving dara-SC and dara-IV.

Adverse event management costs

Frequency of adverse events was derived from clinical trials and costs per event taken from literature [4,5] or national DRG tariff [6].

Productivity loss

It captures the productivity loss of both patients and caregiver because of time required for drug administration. Costs associated with productivity loss were estimated based on the median number of hours required for administration and monitoring of daratumumab SC and IV. The time required for the administration of daratumumab was valued according to a published methodology [8]. It was assumed that 72% of patients requiring SC administration and 81% of patients requiring IV administration were accompanied by a caregiver [9].

Table 3. Resources saved for a cohort of 100 patients followed for 3 years switching 95% of patients to dara-SC

	NDMM ineligible for ASCT		NDMM eligible for ASCT	RRMM		RRMM ≥3PLs
	DVMP	DRd	DVTd	DRd	DVd	Dara
Administration	€ 854,317	€ 964,613	€ 378,136	€ 928,791	€ 646,870	€ 345,515
Adverse event	€ 31,952	€ 6,687	€ 6,846	€ 52,164	€ 19,584	€ 7,830
Productivity loss	€ 151,682	€ 175,903	€ 100,553	€ 208,714	€ 156,096	€ 61,730
Total	**€ 1,037,951**	**€ 1,147,203**	**€ 485,535**	**€ 1,189,669**	**€ 822,550**	**€ 415,076**

Abbreviations: **ASCT** = autologous stem cell transplant; **DRd** =daratumumab in combination with lenalidomide and dexamethasone; **DVd** = daratumumab in combination with bortezomib and dexamethasone; **DVMP** = daratumumab in combination with bortezomib, melphalan and prednisone; **DVTd** = daratumumab in combination with bortezomib, thalidomide and dexamethasone; **IA3** = interim analysis 3; **IV** = intravenous; **N/A** = not applicable; **NDMM** = newly diagnosed multiple myeloma; **PL** = prior line; **RRMM** = relapsed/refractory multiple myeloma; **SC** = subcutaneous; **TTD** = time-to-treatment discontinuation.

CAVEAT: *DRd, DVd and Dara monotherapy data have been updated to the latest available cut-off following abstract submission*