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COMPARATIVE ENVIRONMENTAL IMPACT ASSESSMENT OF INTRAVENUOUS AND SUBCUTANUOUS DARATUMUMAB ADMINISTRATION IN ITALY: AN APPLIED CASE STUDY

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Objective

- Healthcare systems around the world play a critical role in enhancing human development, but also contribute to carbon emissions: if the healthcare sector were a nation, it is estimated that it would rank as the fifth-largest emitter globally [1].
- Daratumumab, used for treating multiple myeloma (MM), is available in subcutaneous (SC) and intravenous (IV) formulations, with the SC version offering advantages in terms of administration time, tolerability and costs for hospitals, patients, and society [2, 3].
- This study represents the first one of its kind to evaluate the carbon footprint of the early development of the SC formulation of daratumumab within the Italian healthcare context, considering worst-, and best-case scenarios.

Methods

- Following Life Cycle Assessment (LCA) principles, we developed an Environmental Impact Model to estimate the annual carbon footprint of SC and IV formulations of daratumumab. This was expressed in carbon dioxide equivalent (CO_2eq).
- The functional unit was defined as a hospital administration of daratumumab for the treatment of adult MM patients.
- For every phase of the product life cycle (Figure 1), we identified factors differentiating the IV and SC formulations of daratumumab in terms of CO_2eq emissions. For this analysis, in the absence of specific information and considering that the active pharmaceutical ingredient is the same for both formulations, we did not consider the emissions related to drug production.
- Differential factors:
  - The recommended daratumumab dose is 16 mg/kg body weight for IV formulation and 1,800 mg for the SC formulation [4]. The ratio between IV and SC formulations for an average patient weight of 70 kg was estimated to be three-to-one vials per administration.
  - Duration, working time and use of disposables for drug preparing and administration.
- Similarities: pack size, packaging materials, production site, distribution logistics, storage conditions, and waste disposal protocols.
- Data on resource consumption were collected using local or European real-world data, supplemented by expert opinions where data were lacking.
- Resource consumption was then converted into CO_2eq emissions applying established conversion factors from institutional sources.
- For single functional unit, inventory and assessment are described below; worst- and best-cases settings are detailed in supplementary material.

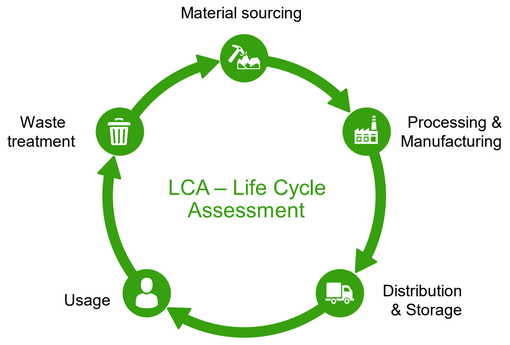

Figure 1 – Life cycle assessment

- The packaging of daratumumab, irrespective of formulation, consists of a cardboard box and a type I glass vial with an elastomer stopper and aluminum flip-off seal, along with an information leaflet included in each pack.
- We estimated the weight of each material, excluding the elastomer and aluminum due to their negligible impact.
- **Cardboard/paper: 0.42 g of CO_2eq/g used** [5,6]
- **Glass: 0.57 g of CO_2eq/g used** [5,6]

- The supply chain starts at the production site in Switzerland, with a travel of 2,191 km to reach Italian patients. The drug must be stored between 2°C to 8°C throughout the process.
- A roundtrip and 4,000 packs load, delivered by vans weighing up to 1,305 t, were assumed. During the return trip, the vehicle was assumed to be empty.
- In line with internal data, we assumed that the SC formulation reduces shipping trips from the production site to Italy by 43% and within Italy by 34%.
- **Distribution (full van): 213.42 g of CO_2eq/km travelled** [5,7,8]
- **Distribution (empty van): 164.58 g of CO_2eq/km travelled** [5]
- **Storage: 8.01 g of CO_2eq/vial stored** [9]

- A recent time and motion study [2] showed that the IV formulation was associated with more intensive consumption of supplies compared to the SC formulation.
- We applied the principles of full costing to estimate emissions, therefore also fixed components of emissions were considered. Overhead emissions were estimated with a top-down approach and were allocated to IV and SC formulations based on medical full-time equivalents (FTE) intensity.
- **Medical supplies: 0.31 g of CO_2eq/€ spent** [10]
- **Drugs: 0.37 g of CO_2eq/€ spent** [10]
- **Overhead emissions: 229.26 g of CO_2eq/minute of medical workers** [9,11,12]

- The conversion factor used for medical supplies encompassed waste treatment. Therefore, to avoid double counting, in this phase we focused only on waste generated from daratumumab leftover and its packaging.
- For daratumumab waste disposal, considering an average bodyweight of 70 kg, IV dosage scheme results in a wastage equivalent to 80 milligrams per administration.
- According to Italian regulations, glass and cardboard/paper, when free from bio-hazardous contamination, must be recycled.
- **Drug disposal: 0.38 g of CO_2eq/g of drug** [6]
- **Cardboard/paper recycling: 0.93 g of CO_2eq/g used** [6]
- **Glass recycling: 0.45 g of CO_2eq/g used** [6]

Results

- Life cycle emissions per administration of IV and SC daratumumab were estimated at 23.8 kg of CO_2eq and 10.6 kg of CO_2eq, respectively (Figure 2).
- Key factors influencing these results included the allocation of overhead emissions, emissions per euro spent on medical supplies, reduction in delivery trips, and emissions related to drug packaging.
- On a national scale, total emissions savings depended on the number of patients treated with the SC formulation and the timing of its development. **The early development of the SC formulation resulted in annual emissions savings for Italy ranging from 123 to 3,192 t of CO_2eq every 1,000 MM patients treated** (Figure 3).

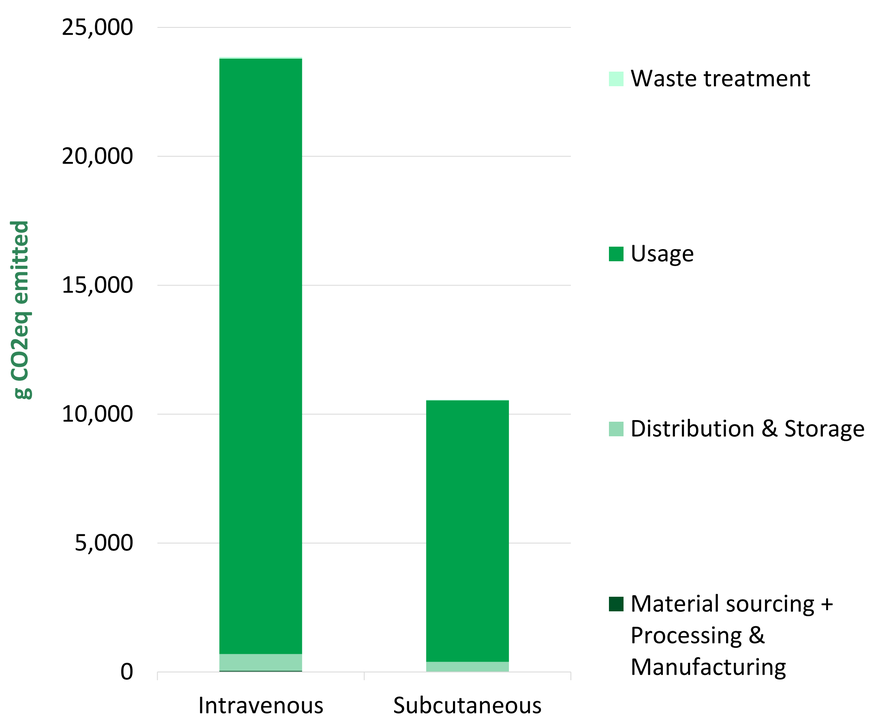

Figure 2 – Summary results

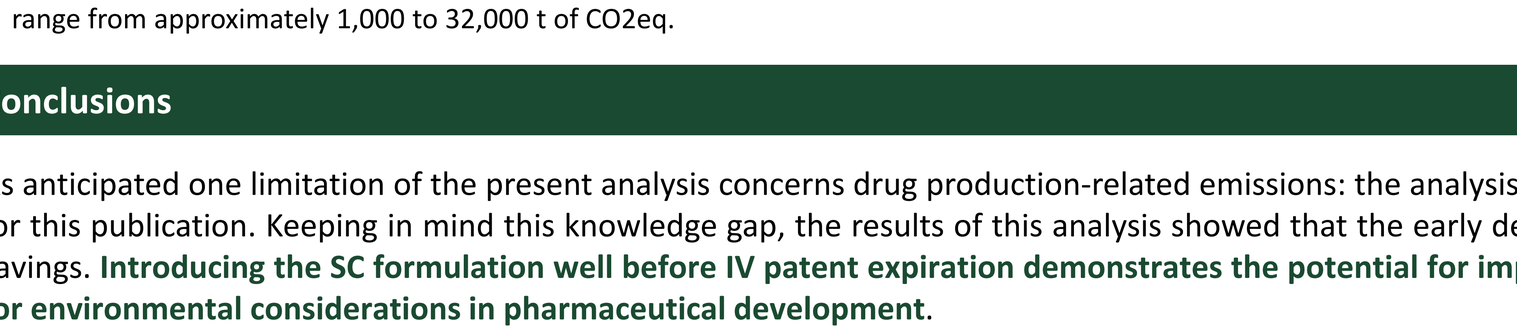

Figure 3 – Results for worst and best case

- Considering the SC formulation was introduced 10 years before IV patent expiration, overall savings were projected to range from approximately 1,000 to 32,000 t of CO_2eq.

Conclusions

As anticipated one limitation of the present analysis concerns drug production-related emissions: the analysis of this factor was still on-going when current results were finalized for this publication. Keeping in mind this knowledge gap, the results of this analysis showed that the early development of daratumumab SC formulation brought about CO_2eq savings. **Introducing the SC formulation well before IV patent expiration demonstrates the potential for improving the long-term carbon emissions and emphasizes the need for environmental considerations in pharmaceutical development**.

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ISPOR Barcelona 2024

Acknowledgements This analysis was funded by Johnson & Johnson