#EE31

A Systematic Literature Review of Adherence and Economic Burden Associated With Subcutaneous Versus Intravenous Oncology Therapies

Casañas i Comabella C,[1*] Burnett H,[2] Nguyen V,[3] Sarocco P,[4] Epstein RS[5]

*[1]Evidera Ltd., a business unit of PPD, part of Thermo Fisher Scientific, London, UK; [2]Evidera Inc., a business unit of PPD, part of Thermo Fisher Scientific, Montreal, Canada; [3]Evidera Ltd., a business unit of PPD, part of Thermo Fisher Scientific, Paris, France; [4]Halozyme Therapeutics, Inc., San Diego, CA, USA; [5]Epstein Health, LLC, Woodcliff Lake, NJ, USA; *Presenting Author*

Background and Objective

- Traditional intravenous (IV) cancer treatments require lengthy infusion times, thus contributing to the burden on healthcare resources and costs. In contrast, numerous studies have consistently demonstrated that subcutaneous (SC) treatments for cancer have comparable or superior effectiveness and safety to IV[1-6] and could reduce the burden on healthcare systems.[7,8] However, such studies did not report head-to-head comparisons.
- Evidence consistently demonstrates that SC administration is associated with improved quality of life and patient preference, including several literature reviews[1,9,10] that reported that up to 88.9% of cancer patients preferred administration by SC over IV.[11]
- It was therefore of interest to systematically identify and summarize the findings from real-world (RW) studies published in the last 10 years that compared the impact of SC and IV oncology therapies on the economic burden (cost and healthcare resource use [HCRU]) and medication adherence.

Methods

- A systematic literature review (SLR) was performed using recent best practice methods,[12,13] aiming to identify RW studies conducted in Europe and North America that reported head-to-head comparisons of SC and IV oncology therapies in terms of patient adherence, HCRU, and costs. The selection criteria applied are presented in **Table 1**.

Table 1. Study Selection Criteria

Domain	Inclusion criteria
Population	• Adults (≥18 years old) with cancer • Payers (public and private healthcare settings), and healthcare providers of adults with cancer
Interventions	Any SC agent/s in oncology
Comparators	Any IV agent/s in oncology
Outcomes	**Healthcare resource use:** Length of stay/clinic time/chair time, medical/nurse staff active time, healthcare visits (frequency, mean/median number) **Costs:** Direct (e.g., overall, related to specific resource use) and indirect (e.g., productivity loss, absenteeism, opportunity loss, transportation time) **Patient adherence/compliance:** Rates (%), missed appointments/cancellations by patient, refusal to treatment, adherence scales
Study design	Prospective cohort or cross-sectional studies, and retrospective/claim-based studies

IV = intravenous; SC = subcutaneous

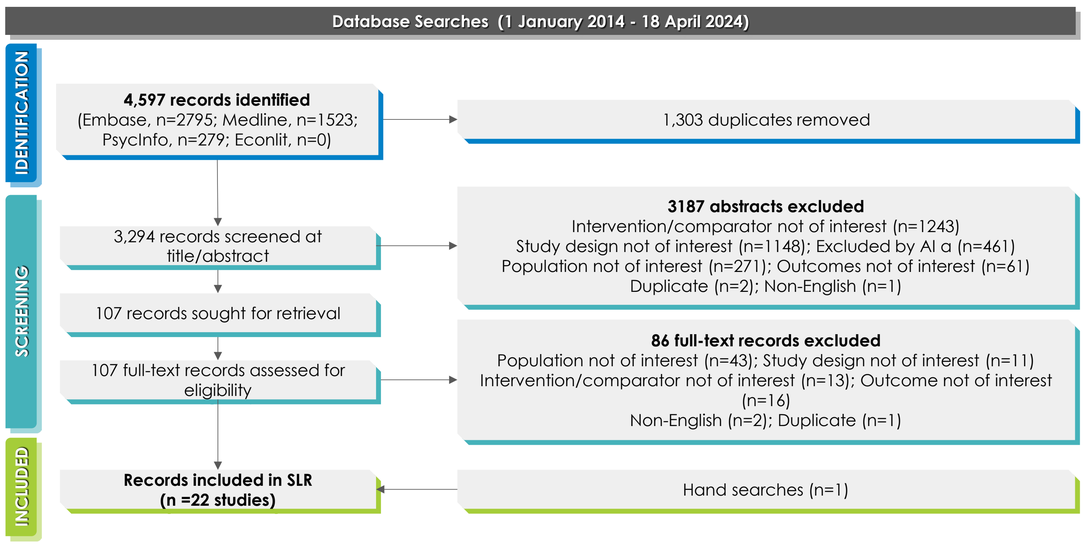
- Searches were conducted in Embase, MEDLINE, EconLit, and PsycINFO for studies published between January 2014 and April 2024.
- Titles and abstracts were screened independently by a human reviewer and by artificial intelligence algorithms via Nested Knowledge, and conflicts were addressed by the human reviewer. Abstracts meeting the selection criteria proceeded to full-text screening by two human reviewers, and conflicts were resolved by a third reviewer. Reasons for exclusion were recorded.
- Data extraction was conducted by one reviewer and validated by a second.

Results

Summary of Included Studies

- The SLR identified a total of 22 studies, of which 21 were identified via database searches and one via hand searching of bibliographies (**Figure 1**).

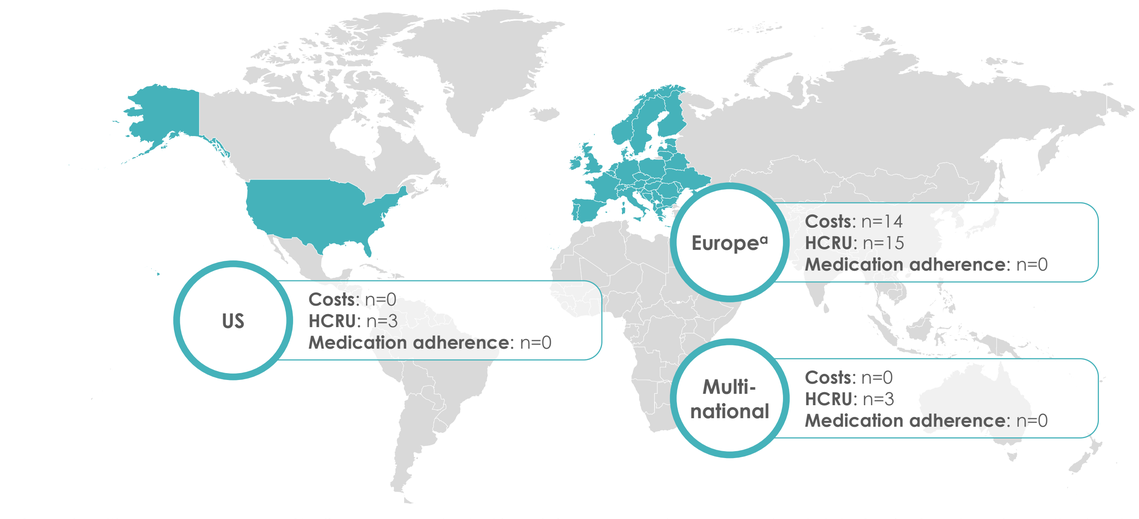
Figure 1. Number of studies by topic and geography (n=22)*



*All records allocated a low probability of advancement by AI were cross checked by a human screener.

- An overview of included studies is presented in **Figure 2**. Most studies were conducted in Europe (n=16), three in the US, and three were multinational (**Figures 2 and 3**). The distribution of studies by cancer type is shown in **Figure 3**. Most studies assessed trastuzumab or rituximab (**Figure 4**).

Figure 2. Overview of included studies by geography (n=22)

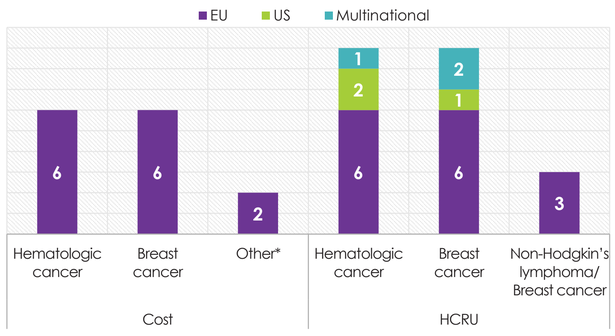


HCRU = healthcare resource use; [a]Studies were conducted in Belgium, Denmark, France, Ireland, Italy, Spain, Sweden, The Netherlands, UK

- All treatments were administered by healthcare professionals (HCPs).
- Nearly all studies reported on HCRU (n=21), and 14 studies reported on cost. No studies were identified that compared adherence to anti-cancer therapies by patients receiving SC versus IV medication.

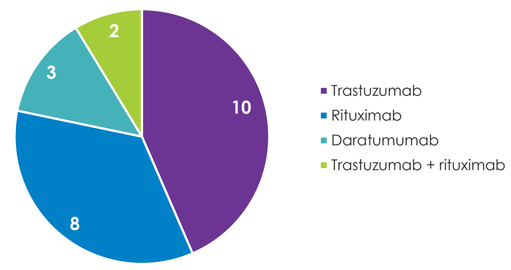
Results (cont.)

Figure 3. Number of studies by topic and geography (n=22)*



*Counts do not add to 22 because studies reported multiple outcome categories of interest.

Figure 4. Number of studies by cancer treatment (n=22)*



*Counts do not add to 22 because one study reported rituximab and trastuzumab separately.

Costs

- All studies that evaluated costs were from Europe (n=14); none were conducted in the US. All studies reported costs savings of SC versus IV administration.
- In all six studies assessing trastuzumab SC had significantly lower direct costs than IV.[14-19] One study reported that SC trastuzumab saved €1,132.43 in indirect costs.[15] A study in Sweden showed that the use of SC saved €603,000 in annual direct costs by avoiding surgeries to implant port-a-caths and pharmacy fees for the reconstitution of IV doses, and use of less expensive materials with SC.[14] In patients with breast cancer receiving SC trastuzumab saved a mean €6,057 (94% saving) vs IV per patient per year in drug wastage.[20]
- SC rituximab also saved costs compared with IV administration because of lower treatment costs in patients with hematologic cancers,[21-24] and one study reported a median cost reduction of 25.4%.[21] In patients with non-Hodgkin's lymphoma, SC rituximab saved a mean €28,399 (100% saving) vs IV per patient per year in drug wastage.[20]
- SC daratumumab was investigated in two studies on multiple myeloma,[25,26] with a French study reporting savings of €29,460 in treatment costs compared to IV,[25] and an Italian study showed a 51.6% cost reduction with SC compared to IV.[26]

HCRU Europe

- All 21 studies consistently reported reductions in HCRU when using SC versus IV administration, regardless of geography.

European Studies (n=15)

- **Time spent in hospital/chair time:** An 80% reduction in patient chair time was reported for breast cancer patients receiving trastuzumab, from 101 minutes (IV) to 20 minutes (SC),[15] and SC rituximab reduced chair time by a mean of 193.8 minutes in patients with non-Hodgkin's lymphoma compared with IV.[24] Time spent in hospital was reduced by 101 minutes for the first visit and 23 minutes for subsequent visits in breast cancer patients receiving SC trastuzumab.[17] Total patient time in the oncology unit was 71% shorter for SC trastuzumab vs IV in patients with breast cancer.[19] Compared with IV, SC daratumumab was associated with 78% savings in patient time and 80% savings in infusion chair time in patients with multiple myeloma.[26]
- **HCP time:** HCP time reductions of 50% and 79% were reported with SC trastuzumab vs IV in patients with breast cancer.[15,16] SC rituximab saved a mean of 5.6 minutes per preparation and 11.1 minutes per administration in patients with lymphoma.[22] Similar findings were reported by another study where mean pharmacy nurse preparation time was reduced by 50% by dose (5 minutes with SC vs 10 minutes with IV).[21] The median time of occupation of the day care unit was 1 hour with SC vs 4 hours (1-7) with IV.[21] In another study, SC rituximab cut a total of 174.8 minutes (95% CI: 172.5–177.1) of active HCP time per session (i.e., roughly 3 hours) vs IV.[24] Two studies in multiple myeloma reported savings: SC daratumumab had a shorter infusion time (4–6 minutes for SC vs. 240–360 minutes for IV),[25] and saved 59% HCP active working time over IV.[26]

HCRU US and Multinational Studies

US Studies (n=3)

- All US studies reported savings, including patient's chair time and clinic time.
- One study with patients with lymphoma and leukemia SC receiving rituximab showed significantly reduced therapy chair time vs IV by a mean 62% (133.4 minutes; $P<0.001$).[27] Another study on daratumumab for multiple myeloma reported savings in median total clinic time (2.7–3.0 hours shorter for SC vs IV) and median total chair time (2.7–2.8 hours shorter for SC vs IV).[28]

Multinational Studies (n=3)

- An international study on rituximab for lymphoma reported a 74% reduction in mean chair time and a 32% reduction in HCP time with SC vs IV across countries.[29] SC trastuzumab significantly reduced patient chair time: 73.1% reduction with a single-use SC injection device (20.9 minutes for SC vs. 77.8 minutes for IV, $P<0.0001$) and 71.0% reduction with an handheld SC syringe (22.6 minutes, $P<0.0001$).[30] Another international study reported SC trastuzumab saved patient chair time from 68% in France and Canada to 80% in Spain, and consistently saved HCP time vs IV by 30% to 51% across six European countries.[31]

Conclusions

- **Despite the comparable effectiveness and safety, proven patient preference for and higher satisfaction with SC vs IV, only three US studies examined the impact of SC vs IV on HCRU in head-to-head comparisons, and no US studies compared costs head-to-head. Most evidence was found in European studies. To date, most US studies comparing RW SC and IV administration have focused on effectiveness and safety, which is perhaps to be expected in relatively new treatments. The lack of studies in the US may also be linked to the underutilization of SC in the US.[32]**
- **Given reported HCP's concerns about medication adherence, studies that compare SC and IV medication adherence in cancer are needed globally.**
- **In the US, studies are needed to further explore the RW impact of SC dosing on reducing economic burden (costs and HCRU), especially with new and increasingly larger biologic injectables entering the market, to inform improved policy decision-making and clinical awareness.**

References

1. Anderson KC, et al. *Future Oncol*. 2019;15(28):3267-81.
2. De Sanctis R, et al. *Breast*. 2021;57:80-85.
3. Minarik J, et al. *PLoS One*. 2015;10(4):e0123866.
4. Rotkopf H, et al. *Clin Lymphoma Myeloma Leuk*. 2021;21(1):e32-e38.
5. Sidana S, et al. *PLoS One*. 2017;12(3):e0172996.
6. Visentin A, et al. *Curr Oncol*. 2022;[30](1):274-83.
7. Hansen RN, et al. *Value Health*. 2018;21(suppl 1):S22-S23.
8. Rojas L, et al. *PLoS One*. 2020;15(2):e0227961.
9. Landeiro LCG, et al. *Front Pharmacol*. 2024;15:1338546.
10. Parra A, et al. *Expert Rev Pharmacoecon Outcomes Res*. 2023;23(9):1017-26.
11. Pivot X, et al. *Lancet Oncol*. 2013;14(10):962-70.
12. Higgins JPT, et al., eds. *Cochrane handbook for systematic reviews of interventions (version 6.4)*. 2023.
13. National Institute for Health and Care Excellence. 2024.
14. Hedayati E, et al. *PLoS One*. 2019;14(2):e0211783.
15. Lopez-Vivanco G, et al. *Clin Transl Oncol*. 2017;19(12):1454-61.
16. O'Brien GL, et al. *Clin Breast Cancer*. 2019;19(3):e440-e51.
17. Olofsson S, et al. *Breast*. 2016;29:140-46.
18. Olsen J, et al. *J Comp Eff Res*. 2018;7(5):411-19.
19. Tjalma WAA, et al. *Eur J Obstet Gynecol Reprod Biol*. 2018;221:46-51.
20. Ponzetti et al. *Clinicoecon Outcomes Res*. 2016;8:227-33.
21. Delgado Sanchez O, et al. *Clinicoecon Outcomes Res*. 2019;11:695-701.
22. Fargier E, et al. *Ann Hematol*. 2018;97(1):123-31.
23. Mihajlovic J, et al. *Clin Ther*. 2017;39(6):1221-32 e4.
24. Rule S, et al. *J Med Econ*. 2014;17(7):459-68.
25. Badibouidi F, et al. *Eur J Oncol Pharm*. 2023;6(suppl):26.
26. Pradelli L, et al. *Cancer Med*. 2023;12(23):21480-89.
27. Drill E, et al. *Oncology (Williston Park)*. 2021;35(12):804-11.
28. Soefje SA, et al. *JCO Oncol Pract*. 2023;19(4):e542-e49.
29. De Cock E, et al. *PLoS One*. 2016;11(6):e0157957.
30. De Cock E, et al. *Cancer Med*. 2016;5(3):389-97.
31. Jackisch C, et al. *Geburtshilfe Frauenheilkd*. 2015;75(6):566-73.
32. Tang M, et al. *JAMA Oncol*. 2023;9(5):717-19.

Disclosures

CCC, **BH**, and **VN** are employees of Evidera, a business unit of PPD, part of Thermo Fisher Scientific. **SP** is employed by Halozyme Therapeutics and may own stock in Halozyme Therapeutics, Inc. **ERS** is the CEO and co-founder of Epstein Health, LLC; currently serves on the Boards of Directors of Illumina (ILMN), Fate (FATE) Therapeutics, Veracyte (VCYT), and Proteus Digital Health.

Acknowledgements

This research, as well as medical writing assistance, was funded by Halozyme Therapeutics, Inc. The authors thank Phil Leventhal of PPD, part of Thermo Fisher Scientific for providing scientific writing support. Editorial and graphic design support were provided by Rodney Atkins and Kawthar Nakayima of Evidera, a business unit of PPD, part of Thermo Fisher Scientific.

Scan the QR code for eposter.