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Time to Approval of Chimeric Antigen Receptor-T Cells (CAR-T) Therapies among Nordic Countries

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BACKGROUND

- Chimeric Antigen Receptor-T Cell (CAR-T) therapy is a cell-based gene therapy designed to attack cancer cell antigens, specifically in patients with relapsed/refractory (R/R) B-cell malignancies.
- To date, six CAR-T therapies have been approved by the European Medicines Agency (EMA) across different indications (**Table 1**).

OBJECTIVE

- This study examined the time to approval for six CAR-T therapies in four Nordic countries (Denmark, Finland, Norway and Sweden), after authorization by the EMA.

Table 1. EMA CAR-T marketing authorizations

CAR-T	Indication	Date of EMA marketing authorization
Tisagenlecleucel (Kymriah®)	B-ALL R/R (≥2L)* Adult DLBCL R/R (≥2L) Adult FL R/R (≥2L)	Aug 23, 2018 Aug 23, 2018 Apr 29, 2022
Axicabtagene ciloleucel (Yescarta®)	Adult DLBCL R/R (≥2L) Adult PMBCL R/R (≥2L) Adult FL R/R (≥3L) Adult HGBL/DLBCL R/R (>1L)	Aug 23, 2018 Aug 23, 2018 Apr 22, 2022 Sep 15, 2022
Brexucabtagene autoleucel (Tecartus®)	Adult MCL R/R (≥2L) B-ALL R/R¥	Dec 14, 2020 Jul 21, 2022
Idecabtagene vicleucel (Abecma®)	Adult MM R/R (≥4L)	Aug 18, 2021
Lisocabtagene maraleucel (Breyanzi®)	Adult DLBCL R/R (≥2L) Adult PMBCL R/R (≥2L) Adult FL R/R (grade 3B) (≥2L)	Apr 04, 2022 Apr 04, 2022 Apr 04, 2022
Ciltacabtagene autoleucel (Carvykti®)	Adult MM R/R (≥3L)	May 25, 2022

>1L, after first line systemic therapy, ≥2L, second line or later systemic therapy; ≥3L, third line or later systemic therapy; ≥4L, fourth line or later systemic therapy; B-ALL, b cell-acute lymphoblastic leukemia; DLBCL, diffuse large B-cell lymphoma; HGBL, high-grade B-cell lymphoma; FL, follicular lymphoma; PMBCL, primary mediastinal large B-cell lymphoma; MCL, mantle cell lymphoma; MM, multiple myeloma.

* Pediatric and adults ≤ 25 years of age with B-ALL.
¥ Adults ≥ 26 years with R/R B-ALL

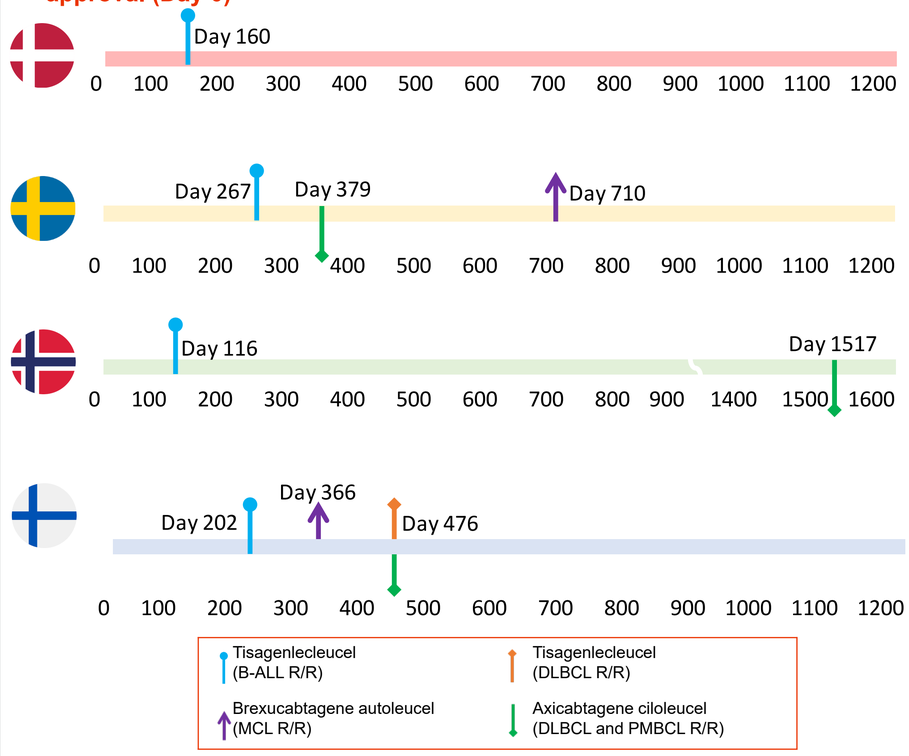
METHODS

- CAR-T therapies authorized by the EMA before January 1, 2023, were identified using European Public Assessment Reports (EPARs).
- Country-specific approval dates were identified from published reports of health agencies in four Nordic countries:
  - Danish Medicines Council
  - Council for Choices in Health Care (Finland)
  - Norwegian Medicines Agency
  - NT Council/Dental and Pharmaceutical Benefits Agency (Sweden)
- Time to approval, for each indication after EMA authorization, was estimated for each country.

RESULTS

- Tisagenlecleucel was approved for R/R pediatric and young adults ALL (up to 25 years of age) within a year of EMA approval for all included countries.
  - Norway (116 days), Denmark (160 days), Finland (202 days) and Sweden (267 days) after EMA approval
- Tisagenlecleucel was approved for adult DLBCL in Finland (476 days after EMA approval) and rejected by other countries since the therapy was considered as not cost-effective.
- Axicabtagene ciloleucel was approved in most Nordic countries (not Denmark) for R/R adult patients with DLBCL and PMBCL, after 2 or more lines of systemic therapy.
  - Sweden (379 days), Finland (476 days) and Norway (1,517 days) after EMA approval for the indication.
- Brexucabtagene autoleucel was approved for adult MCL in Finland (366 days) and Sweden (710 days) after EMA approval.
  - Brexucabtagene autoleucel is undergoing assessment in Norway for MCL Assessments of other CAR-Ts in Table 1 are ongoing for multiple indications in all listed countries.
  - In Sweden, negotiations are currently paused by companies for Idecabtagene vicleucel and Lisocabtagene maraleucel due to limited manufacturing capacity.

Figure 1. Timelines for CAR-T approvals in Nordic countries from EMA approval (Day 0)



CONCLUSIONS

- There are considerable differences in the time for CAR-T therapy approval among Nordic countries (116 to 1,517 days), after marketing authorization by the EMA.
  - This study did not consider when companies applied for authorizations in the chosen countries. Therefore, the presented results may include application process delays.
  - Difference in time to approval among countries was shortest for Tisagenlecleucel for B-ALL R/R (116-267 days).
- Conflicting outcomes (approval vs. rejection) and approval delays may result in barriers to patient access across the Nordic region.

REFERENCES

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