SIOP Europe
the European Society for Paediatric Oncology

ACCELERATE
INNOVATION FOR CHILDREN AND ADOLESCENTS WITH CANCER

HTA : The current paediatric challenges in the EU and perspectives

Gilles Vassal,

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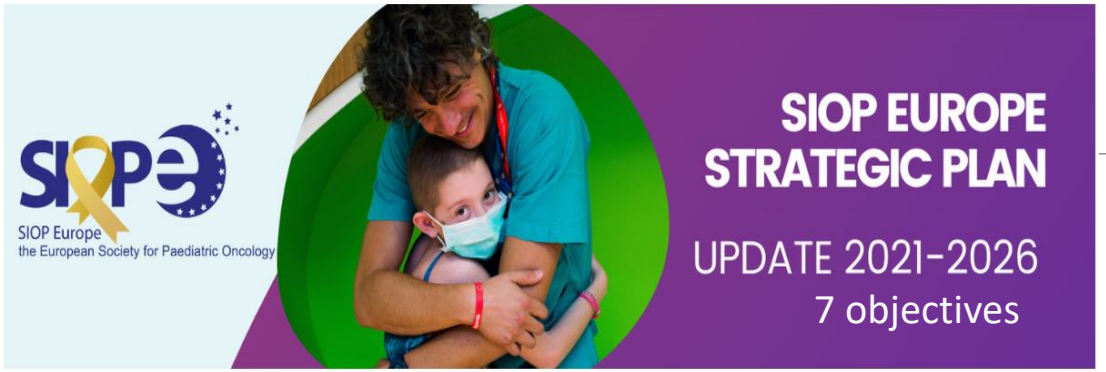
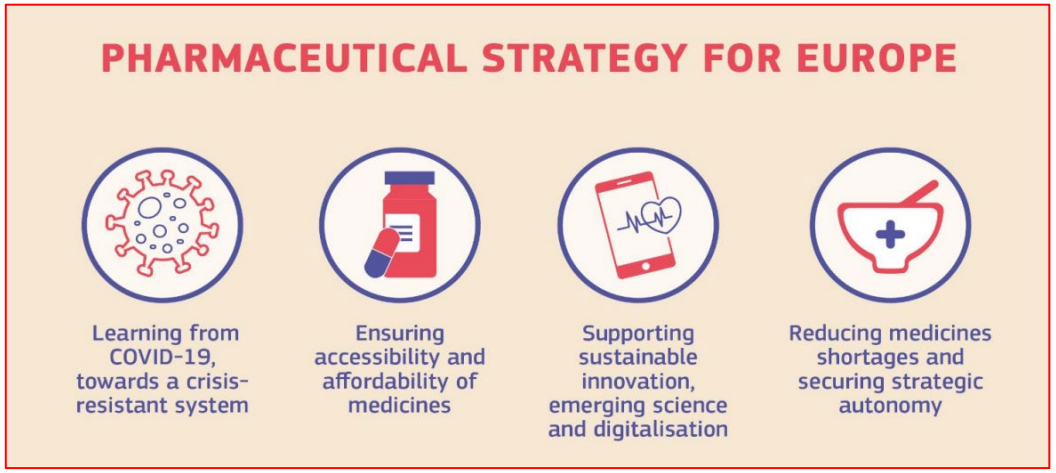


Objective 1 : Addressing Inequalities
to bring about equal access to standard care, expertise and clinical research for diagnosis, treatment and follow-up across Europe and to promote patient involvement and a patient-centred approach throughout



New legal framework:
general pharmaceutical legislation, revised pediatric and orphan regulations

HTA regulation (to be launched in Jan 2025**)**

Challenges

- Children experience delay in access to new anticancer medicines
- Childhood cancers are (ultra) rare diseases
- Paediatric oncology community not aware of Health Technology Assessments

- Goal : Generate data and proposed solutions

Project

1. Generate data

- Study HTA evaluations for 3 anticancer medicines, recently indicated for paediatric use

- Explore origin of delay and discrepancies

- Survey experience end-users

2. ACCELERATE Multistakeholder discussion to propose solutions

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ScienceDirect

journal homepage: www.ejcancer.com

Original Research

Market access to new anticancer medicines for children and adolescents with cancer in Europe

Reineke A. Schoot [a], Maria A. Otth [b,c], Gerardus W.J. Frederix [d], Hubert G.M. Leufkens [e,1], Gilles Vassal [f,1,*]

And Eva Brack, Marko Okocolojic

From the SIOPE Access Working Group

Selection of medicines

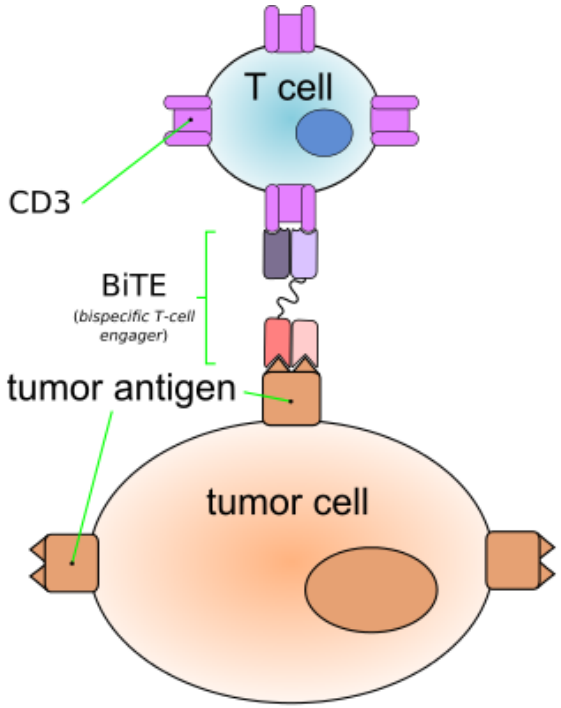
- New molecular entities, paediatric indication granted > 2007 but < 2019
- Criteria:

1. relevance
2. first approval in children vs pediatric variation already approved medicine,
3. (high) price and expected budget impact

- Decided to leave out tissue agnostic indications for now

Blinatumomab (Blincyto™)

- Bispecific T-cell engager (CD19 - CD3)
- Dismal prognosis relapsed/refractory BCP-ALL
- Phase 2: CR in 39% (27/70 pts)[1]
- Selection
  - ✓Relevance: ALL largest population
  - ✓First approved in adults
  - ✓Considerable budget impact (patient numbers)

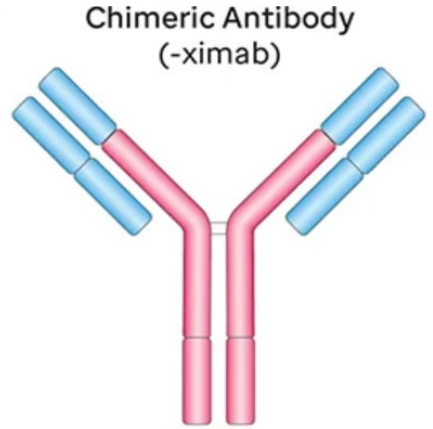


Pediatric EU approval in august 2018

[1]Von Stackelberg JCO 2016

Dinutuximab beta (Qarziba™)

- Monoclonal antibody GD2
- USA: Unituxin™ EFS 46% -> 66%[1]
- EU: Qarziba™ similar EFS[2]
- Selection
  - ✓Relevance: practive changing in the treatment of high-risk neuroblastoma
  - ✓First approved in children

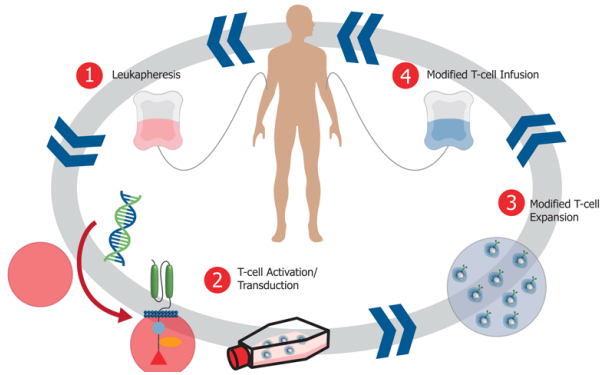


Pediatric EU approval in may 2017

[1]Yu NEJM 2010, [2]Ladenstein Lancet Oncol 2018

Tisagenlecleucel (Kymriah™)

- (autologous) CAR T cells CD19
- Dismal prognosis relapsed/refractory BCP-ALL
- 18 mo RFS 66% and OS 70%[1]
- Selection
  - ✓Relevance: ALL largest population, new type of treatment
  - ✓First approved in children
  - ✓Considerable budget impact (high price)



Pediatric EU approval in august 2018

[1]Grupp Blood 2018

Method

- Reports:
  - ✓HTA reports public domain
  - ✓April 2020 – November 2020
  - ✓9 EU countries (≥1 report)
  - ✓Data extraction 2 authors
  - ✓Translation online

- Data: nature HTA decision, timelines

Method survey

- Online survey
- Representatives of National Pediatric Hemato-Oncology societies (NAPHOS)

- Questions:
  I. HTA in your country?

  For each of the 3 medicines:
  I. Are you able to prescribe this medicine in your country?
  II. How are the costs covered?

HTA reports

	Blinatumomab	Tisagenlecleucel	Dinituximab beta
UK	Adult report only	+	+
Scotland	+	+	+
Poland	Adult report only	-	+
Norway	Adult report only	+	+
Netherlands	Add-on list	+	+
Italy	+	+	+
Ireland	+	-	-
Germany	+	+	+
France	+	+	+

Recommendations: blinatumomab

	UK	Scotland	Poland	Norway	NL	Italy	Ireland	Germany	France
Blinatumomab									
Recommendation	Adult	+	Adult	Adult	NA	+	+	+	+
Restrictions	-	-	-	-	-	-	-	-	-
Evaluation		?				€	?	*	

R; restrictions, NF; not found, NA; not available

 Concerns about data, price acceptable € Data convincing, price too high, + Positive decision, + R Positive decision with restriction, - Negative decision, ☑ Data convincing and price acceptable, ? No clear recommendation could be extracted from the reports found.

Recommendations: tisagenlecleucel

	UK	Scotland	Poland	Norway	NL	Italy	Ireland	Germany	France
Tisagenlecleucel									
Recommendation	+	+	-	+	+	+	-	+	+
Restrictions	-	-	-	-	-	-	-	-	-
Evaluation	🔍	☑	🔍	🔍	☑	☑	€	🔍	🔍

R; restrictions, NF; not found, NA; not available

🔍 Concerns about data, price acceptable € Data convincing, price too high, + Positive decision, + R Positive decision with restriction, - Negative decision, ☑ Data convincing and price acceptable, ? No clear recommendation could be extracted from the reports found.

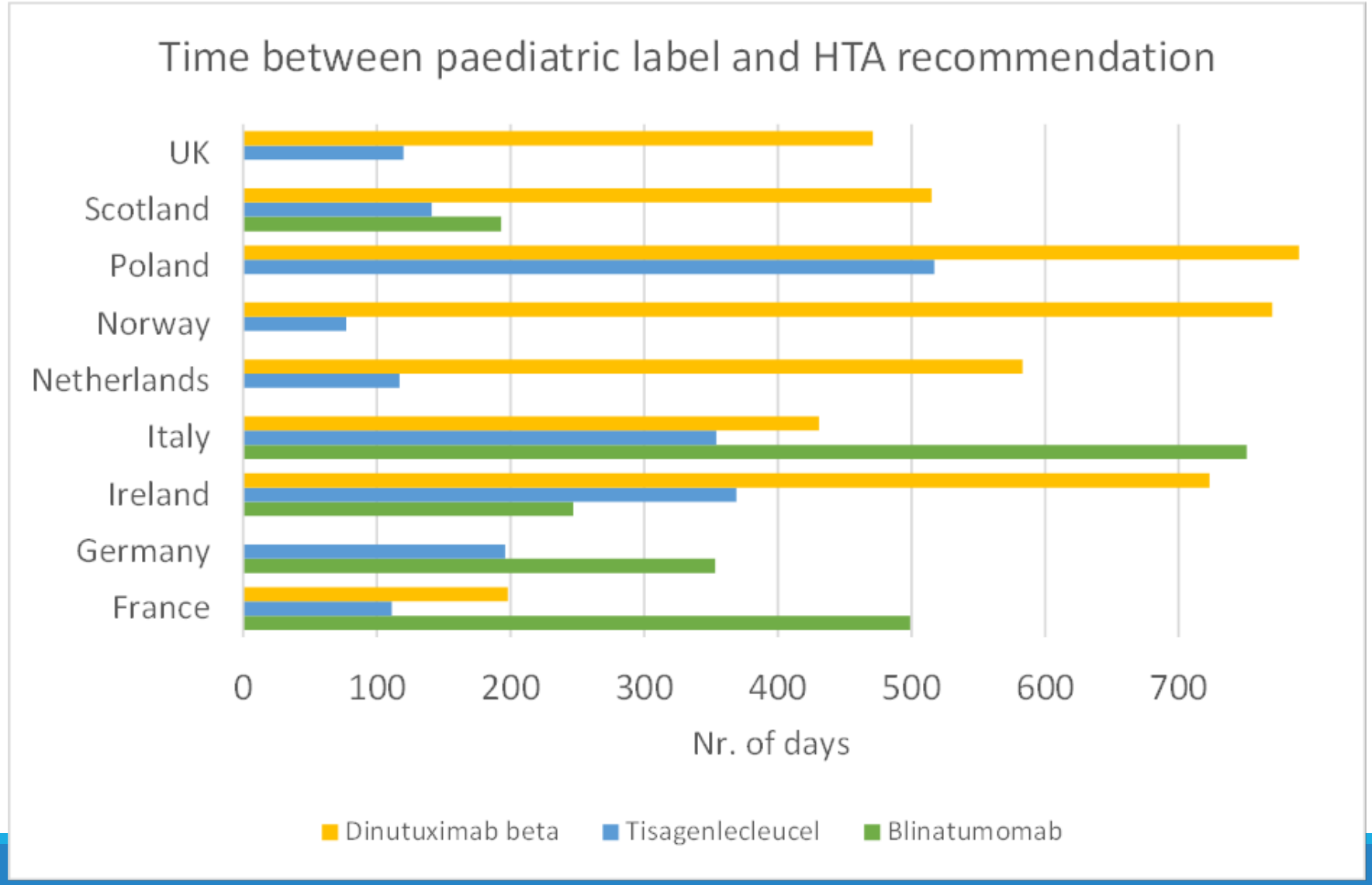
Recommendations: dinutuximab beta

	UK	Scotland	Poland	Norway	NL	Italy	Ireland	Germany	France
Dinutuximab beta									
Recommendation	+ R	+	+	+	+ R	+	-	+	+
Restrictions	No previous dinutuximab, no relapsed or refractory disease	-	-	-	Not for relapsed or refractory disease	-	-	-	-
Evaluation	☑	 €	 €	☑	☑	€	 €	☑	☑

R; restrictions, NF; not found, NA; not available

 Concerns about data, price acceptable € Data convincing, price too high, + Positive decision, + R Positive decision with restriction, - Negative decision, ☑ Data convincing and price acceptable, ? No clear recommendation could be extracted from the reports found.

Time between MA -> HTA approval



Blinatumomab

353 days (193 – 751)

Dinutuximab

515 days (0 - 780)

Tisagenlecleucel

141 days (77 - 369)

Survey of end users

Country	Is there an HTA?	Blinatumomab		Tisagenlecleucel		Dinutuximab beta	
		℞	€	℞	€	℞	€
France	+	+	NHS	+	NHS	+	NHS
Germany	+	+	Insurance	+	Insurance	+	Insurance
Italy	+	+	NHS	+	NHS	+	NHS
Netherlands	+	+	Other	+	Insurance	+	Insurance
Norway	+	+	Hospital	+	Hospital	+	Hospital
Poland	+	+	NHS	-	Charities	+	NHS
UK	+	+	NHS	+	NHS	+	NHS

HTA: health technology assessment

℞ Are you able to prescribe in your country?

€ How are the costs covered?

Conclusion

- Great variability in decision and time between countries
  - ✓Strategy pharmaceutical industry
  - ✓Data requested by HTA
- Limitation: only 3 cases medicines in only 9 countries

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Accelerat-ing robust drug developments to ensure rapid patient- and market- access to newly approved anticancer medicines for the treatment of paediatric malignancies:

An ACCELERATE multistakeholder workshop

January 14, 2022

With representatives from academia, advocacy, EMA, EUnetHTA21, 3 companies

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Patients- and market-access workshop

- Discuss the results of the SIOPE project
- 4 questions:
  - What are good data for HTA evaluation of an asset in a paediatric oncology indication?
  - How assessment could better take into account specificities of paediatric cancers?
  - How to early set up requirements for both regulatory and HTA/Payers evaluation?
  - Could HTA collaboration go beyond clinical assessment?

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6 Proposed Recommendations

1. Early interaction between Industry, EMA, HTA, cooperative groups and advocates at the inception of paediatric development plan.

   This will ensure that there will be alignment, clarity about the required data and ultimately that data will be generated, in a timely fashion, to satisfy all requirements. With this process there would be HTA input into PIP discussions at PDCO.

2. Building academic capability to generate “Real World Data” to satisfy regulatory and HTA requirements

3. Parallel evaluation of paediatric oncology products by EMA (CHMP) and HTAs

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6 Proposed Recommendations

4. Set up obligation and time limits in the revised Paediatric and Orphan regulation to launch products in all member states.
5. Systematic joint clinical assessments for all paediatric oncology products
6. Set up joint procurement and pricing negotiation for all paediatric oncology products

Conclusion

- Need to set up proper health technology assessment of paediatric medicines
- Consider Pediatric Oncology as a regulatory science laboratory for piloting changes and innovation, not limited to the preparation of the implementation of the HTA regulation
- Make pediatric oncologists and advocates aware and knowledgable
- International cooperation