ESTIMATING THE NUMBER OF PATIENTS WITH CHRONIC GRAFT-VERSUS-HOST DISEASE ACROSS EUROPE

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INTRODUCTION

- Chronic graft-versus-host disease (cGVHD) is a major, potentially life-threating complication following allogeneic hematopoietic stem cell transplantation (HSCT) [1].
- Evidence suggests that the 1-, and 5-year cumulative incidence of cGVHD range between 14% and 58%, and 44% and 70%, respectively [2].
- cGVHD typically involves one or more organs including skin, the mucous membrane of mouth, eyes and genitals, the epithelium of gastrointestinal tract, liver, lungs, musculoskeletal system and the hematopoietic systems of bone marrow [3].
- Serious complications caused by cGVHD markedly impair patients' health-related quality of life [4].
- Disease response to currently available immunosuppressive therapies is often slow and limited [5]. Corticosteroids are standard first-line therapy for patients with cGVHD; however, many patients do not respond adequately and need second-line treatment [6]. A better understanding of the cGVHD provides a good opportunity that new therapeutic options will emerge in the near future [2].
- Regardless of the serious consequences of cGVHD, to our knowledge, there are no published estimates of the number of cGVHD patients across Europe.

OBJECTIVES

- **The primary objective of this study was to estimate the number of allogeneic HSCT patients with incident cGVHD annually in France, Germany, Italy, Spain and the UK, and across the EU28 from 2019 to 2023.**
- **Secondary objectives:**
  - **To estimate the annual number of incident cGVHD cases by disease severity and organ involvement;**
  - **To estimate the annual number of steroid-refractory, incident cGVHD cases.**

METHODS

- An epidemiology model was developed in Microsoft Excel 2013 to estimate the annual number of incident cGVHD patients, and cases by disease severity and organ involvement in the EU5 countries and across the EU28 from 2019 to 2023.
- cGVHD was considered according to the National Institutes of Health Consensus Guidelines [7, 8].
- The number of allogeneic HSCT patients was estimated based on country-specific data derived from the annual reports of the European Society for Blood and Marrow Transplantation Registry between 2012 and 2017 [9-14].
- For estimating incident annual cases from 2018 to 2023 linear trend was assumed based on the observed data.
- To collect country/region-specific cGVHD incidence, organ involvement and disease severity data a systematic literature review of English-language articles published between January, 2007 and April, 2019 was conducted using PubMed database.
  - The search strategy was built up as a combination of search strings allowing the capture of all relevant keywords and synonyms that may appear in the potentially relevant papers.
  - The search results were considered in two steps. Initially, the titles and abstracts of all articles were screened and those deemed relevant were analyzed in full text. The literature screening was conducted by two independent reviewers.
  - The literature search was limited to human subject studies applying the National Institutes of Health Consensus Criteria for the diagnosis and staging of cGVHD [7, 8].
  - Data were gathered from text, tables and figures. To collect values from relevant figures the WebPlotDigitizer (version 3.8) software was used.
- In those cases where country-specific data was not available region-specific (EU28) data was used. In those cases where multiple country-specific data sources were available the data used in the model was decided based upon the following criteria:
  - Number of HSCT patients involved in the original study;
  - Number of HSCT centers involved in the original study;
  - The generalizability of the patient population (e.g., studies only with pediatric patients were not used).
- Scenarios estimating steroid-refractory cGVHD cases were also explored assuming that 50% of patients do not respond adequately to first-line corticosteroid therapy [6].

RESULTS

Model inputs

- The literature search for country/region-specific cGVHD incidence, organ involvement and disease severity data resulted in 1,910 hits. The screening identified 17 studies (EU28, n=5; France, n=4; Germany, n=3; Italy, n=3; Spain, n=2; United Kingdom, n=0) reporting relevant data for the model.
- Input data used in the model are presented in **Table 1**.

Estimated annual number of incident cGVHD patients, number of patients by disease severity and organ involvement

- Using the base case inputs, the analysis indicates that the estimated number of incident cGVHD patients in the EU28 will range from 3 218 (mild: 908; moderate: 1 375; severe: 935) to 3 465 (mild: 977; moderate: 1 481; severe: 1 007) between 2019 and 2023 (**Figure 1, Figure 2**).
- The number of incident cGVHD patients shows a similar increasing trend in the EU5 countries (**Figure 3**).
- Our model indicates that the most frequently involved organs in cGVHD are the skin, oral mucosa, eyes, and liver in the EU28 region.
  - Country-specific cGVHD organ involvement data were only available for France; therefore, region-specific data were used for Germany, Italy, Spain and United Kingdom.
  - Based on country-specific data, skin, liver, oral mucosa and gastrointestinal tract are the most frequently affected organs among cGVHD patients in France (**Figure 4**).

Estimated annual number of steroid-refractory, incident cGVHD patients

- Exploratory analysis predicts that due to the higher number of transplantations performed, the number of steroid-refractory patients in the EU28 will likely increase from 1 609 to 1 732 from 2019 to 2023.

Table 1. Model inputs

	EU28	France	Germany	Italy	Spain	United Kingdom
Number of allogeneic HSCT patients						
2012	11 190	1 592	2 866	1 625	886	1 345
2013	11 947	1 724	2 892	1 625	1 072	1 602
2014	12 273	1 805	2 966	1 646	1 061	1 567
2015	12 357	1 816	3 052	1 629	1 069	1 521
2016	12 441	1 845	2 898	1 672	1 096	1 591
2017	12 656	1 731	3 103	1 822	1 115	1 587
1-year cumulative incidence of cGVHD	24%	22%	37%	36%	25%	24%*
cGVHD severity distribution						
Mild cGVHD	28%	23%	27%	28%*	26%	28%*
Moderate cGVHD	43%	40%	30%	43%*	46%	43%*
Severe cGVHD	29%	37%	43%	29%*	28%	29%*
Organ involvement distribution						
Skin cGVHD	72%	60%	72%*	72%*	72%*	72%*
Oral mucosa cGVHD	63%	31%	63%*	63%*	63%*	63%*
Eyes cGVHD	60%	9%	60%*	60%*	60%*	60%*
Liver cGVHD	41%	39%	41%*	41%*	41%*	41%*
Gastrointestinal tract cGVHD	29%	19%	29%*	29%*	29%*	29%*
Lungs cGVHD	32%	2%	32%*	32%*	32%*	32%*
Genitals cGVHD	10%	4%	10%*	10%*	10%*	10%*
Joints and fascia cGVHD	21%	2%	21%*	21%*	21%*	21%*

**Country-specific data was not available region-specific (EU28) data was used*
Input data related to the number of HSCT patients were derived from references: 9-14. Input data related to cGVHD incidence, severity and organ involvement were derived from references 15-22.
HSCT: hematopoietic stem cell transplantation; cGVHD: chronic graft-versus-host disease

Figure 1. Estimated overall number of allogeneic HSCT and incident cGVHD patients in the EU28 from 2019 to 2023

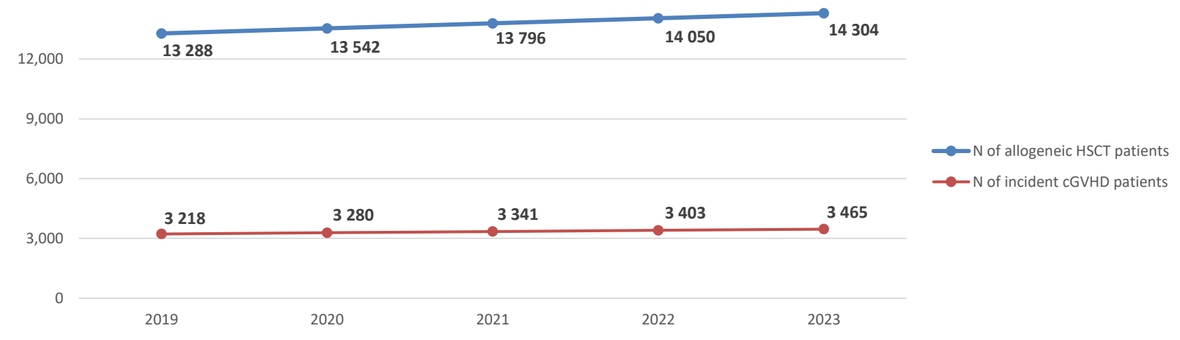


Figure 2. Estimated overall number of incident cGVHD patients by disease severity in the EU28 from 2019 to 2023

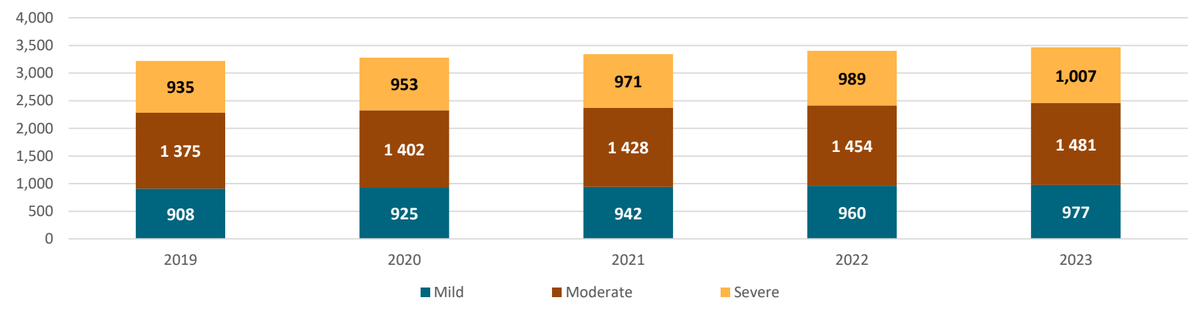


Figure 3. Estimated overall number of incident cGVHD patients by disease severity in the EU5 in 2019 and 2023

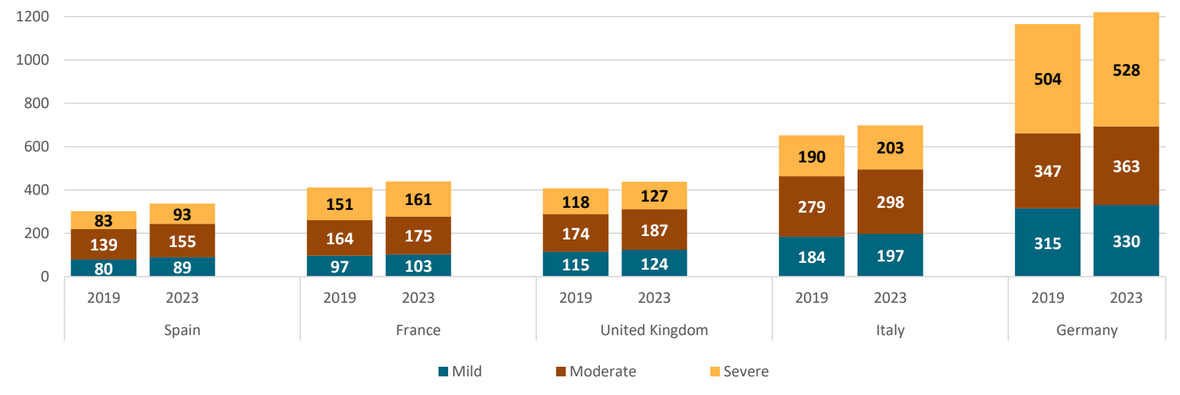
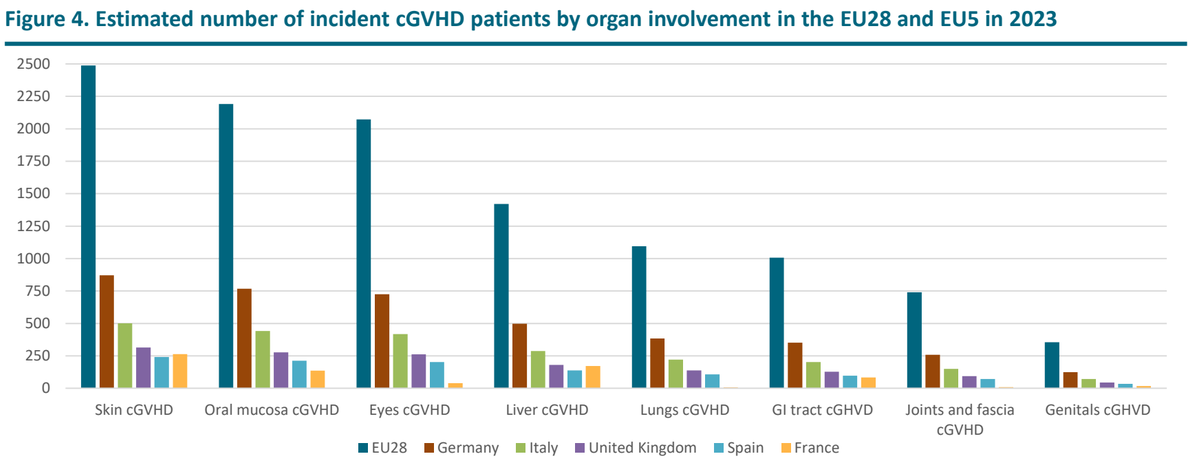


Figure 4. Estimated number of incident cGVHD patients by organ involvement in the EU28 and EU5 in 2023



cGVHD: chronic graft-versus-host disease; GI: gastrointestinal

LIMITATIONS

- The model assumed no changes over time in the incidence of cGVHD.
- Country-specific incidence, disease severity and/or organ involvement data were not available for each EU5 country.
- The model assumed no country specific differences in the incidence of steroid-refractory cGVHD.

CONCLUSIONS

- **With steady growth in allogeneic HSCTs performed in Europe, it can be expected that the number of cGVHD patients will increase by around 7.5% in the next 5 years.**
- **Our findings suggest the majority of diagnosed patients will be moderate or severe.**
- **Considering the high morbidity and impaired quality of life of moderate and severe cGVHD, and the high proportion of resistance to first line treatment, there is a need for effective and tolerable new treatments.**
- **Further comparative studies are recommended to better understand the country-specific differences in the epidemiological data of cGVHD between EU countries.**

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