GENE THERAPIES: THE MOMENT OF TRUTH

ARE PHYSICIANS AND PATIENTS READY?

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Gene therapies are a class of medicines which have the potential to transform how conditions are treated and may even provide a cure. Currently, there are only a handful of gene therapies approved globally; however, this is set to change, with over 1,900 therapies in development from preclinical through to preregistration stage[1], many of which are set to become available to patients in the next few years.

With huge opportunity to offer new hope to patients suffering certain conditions, the pharmaceutical industry continues to invest in the gene therapy market, which is forecast to reach $15.7 billion by 2030, expanding growth at a compound annual growth rate (CAGR) of 20.2% from 2021 to 2030[2].

However, some companies have already experienced challenges including safety setbacks and clinical trial results that fell short of expectations. Furthermore, many patients may not be able to benefit from gene therapies because of challenges with access and funding for these treatments. Timely adoption of gene therapies among stakeholders such as healthcare professionals (HCPs) is a critical element to ensuring the right patients benefit from these treatments. However, data from several Ipsos syndicated Therapy Monitor (TM) and Conference Assessment Studies (see 'About the Research') indicate that HCP awareness of gene therapies is low in some therapy areas and countries and, additionally, that there is hesitancy among some HCPs to use these treatments once they become available. This highlights the need to raise awareness of, and provide further education on, gene therapies.

In the following sections, we use insights from these studies to illustrate examples of knowledge gaps and conclusions as to how these gaps could be bridged.

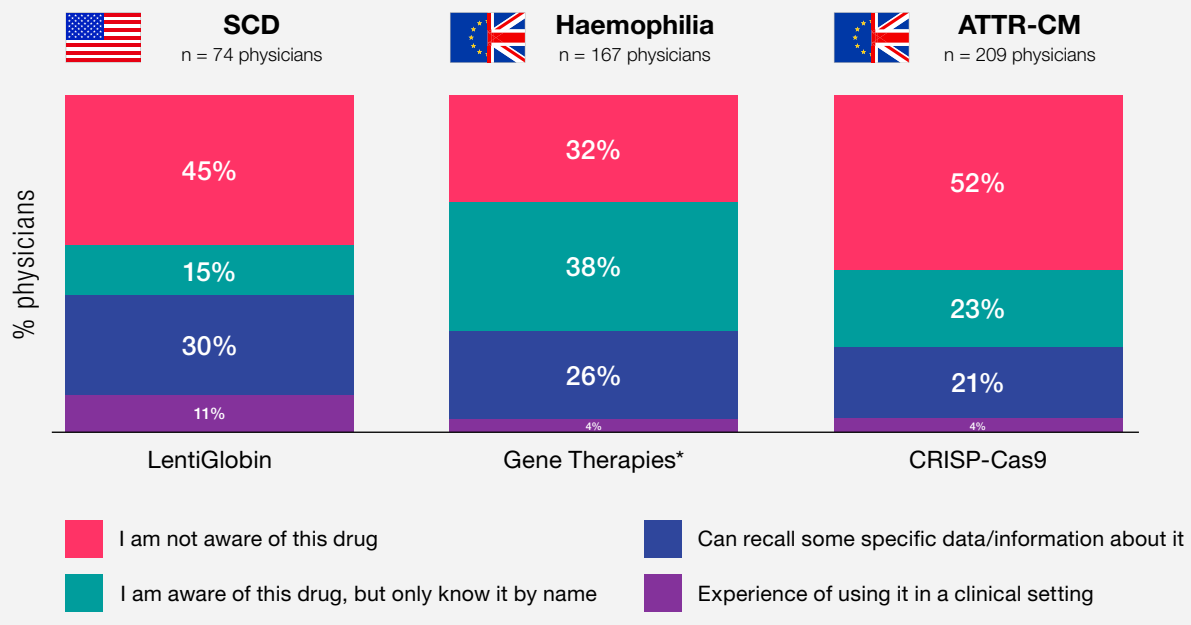
Currently, there are only a handful of gene therapies approved globally; however, this is set to change, with over 1,900 therapies in development[1].

Awareness and level of knowledge of gene therapies in development

Overall, our research shows low prompted awareness among sampled HCPs for some gene therapies in development.

For example, over 1 in 2 (52%) of the cardiologists taking part in Ipsos' Transthyretin Amyloid Cardiomyopathy (AATR-CM) TM in EU4 & UK in Q4 2021 were not aware of CRISPR-Cas9 – a potentially curative gene therapy being developed by Regeneron and Intellia Therapeutics to reverse the gene mutation in ATTR-CM patients. Low awareness was seen even with products in late-stage development, with 45% of the US physicians surveyed in the Q4 2021 Ipsos Sickle Cell Disease TM not aware of Bluebird bio's LentiGlobin gene therapy, a phase 3 pipeline product for sickle cell disease. In addition, almost one third (32%) of the physicians who took part in our Q4 2021 Haemophilia TM in EU4 & UK were not aware (prompted) of haemophilia gene therapies* in development, four out of five of which are in phase 3 clinical development. [FIGURE 1] *(*see 'About the Research' for details of the gene therapies referred to in this article.)*

Figure 1: Prompted awareness of gene therapies in development amongst sampled physicians



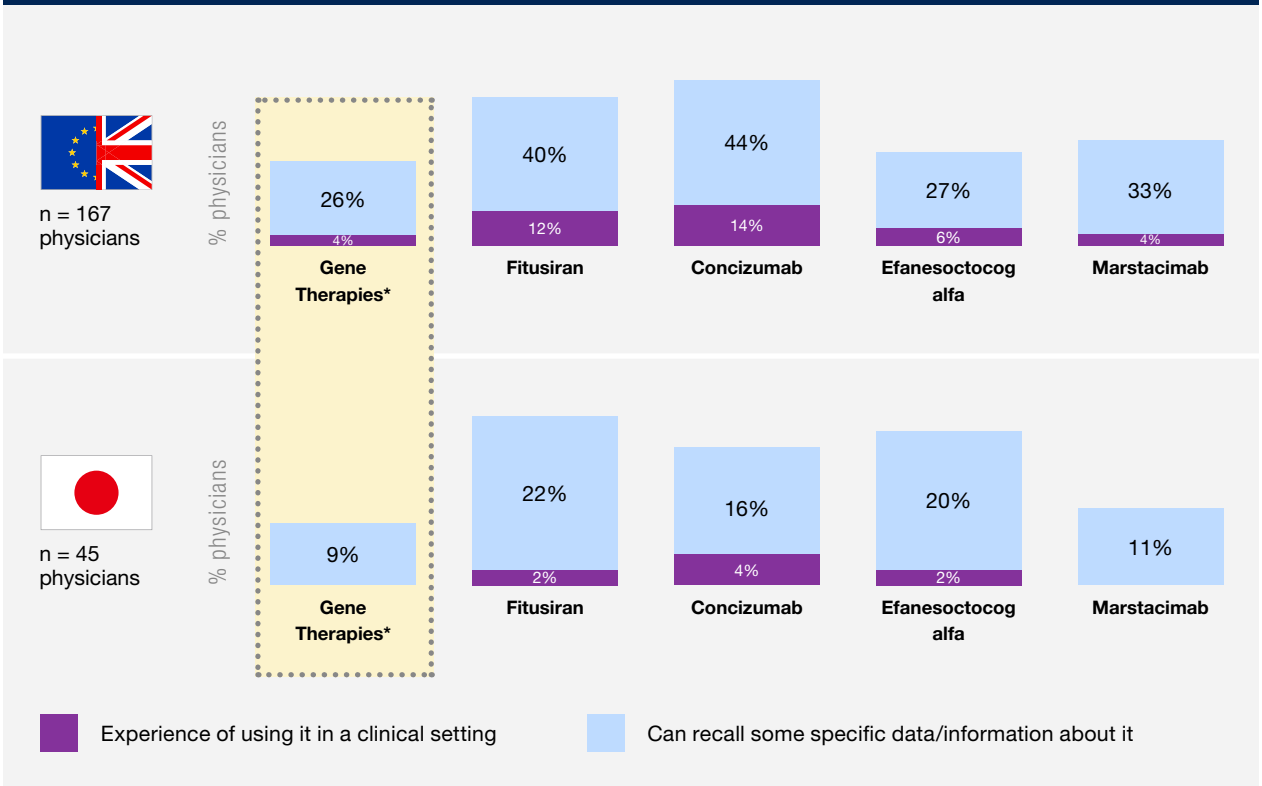
Source: Ipsos Sickle Cell Disease Therapy Monitor (Nov-Dec 2021, 74 physicians in US reporting on 629 patients seen in consultation. Participating physicians were primary treaters and saw a minimum number of SCD patients in the last six months). Ipsos Haemophilia Therapy Monitor (Dec 2021- Feb 2022, 167 EU4 + UK physicians (equal split across countries), reporting on 5-7 haemophilia A patients and 1-2 haemophilia B patients. Participating physicians were primary treaters, spent a minimum amount of time in direct clinical practice, and saw a minimum number of haemophilia patients in the last six months). Ipsos ATTR-CM Therapy Monitor (Nov -Dec 2021, 209 physicians in EU4 +UK (equal split across countries) reporting on 348 patients seen in consultation. Participating physicians were primary treaters, board certified, and saw a minimum number of patients per month). Data collected online. Data © Ipsos 2022, all rights reserved.
*Gene therapies include: valoctocogene roxaparvovec, dirloctocogene samoparvovec, etranacogene dezaparvovec, fidanacogene elaparvovec, giroctocogene fitelparvovec

Overall, our research shows low prompted awareness among sampled HCPs for some gene therapies in development.

Looking at ophthalmology, another category in which clinical studies of promising gene therapies are underway, sampled physicians participating in our Ophthalmology TM had low unprompted awareness of gene therapies in development for neovascular age-related macular degeneration (nAMD), retinal vein occlusion (RVO) and diabetic macular edema (DME). Less than 5% of the ophthalmologists / retinal specialists in our Q4 2021 wave cited unprompted awareness of either 'gene therapies' or named gene therapies in development in EU4 & UK. In addition, unprompted awareness among the same cohort of physicians of the phase 3 gene therapy developmental product, RGX-314 (by Regenxbio and AbbVie for nAMD), was lower than for non-gene therapies at a similar stage of development, e.g., KSI 301, OPT 302 (1% vs 4%, respectively).

Similarly, in our Q4 2021 Haemophilia TM, fewer physicians in EU4, UK and Japan were aware of and familiar with the gene therapies in development (i.e., could either recall some specific data about the product or had used it in a clinical setting) versus the non-gene therapy late-stage pipeline products (e.g., fitusiran, concizumab, efanesoctocog alfa and marstacimab). [FIGURE 2]

Figure 2: Prompted awareness of developmental products for haemophilia amongst sampled physicians

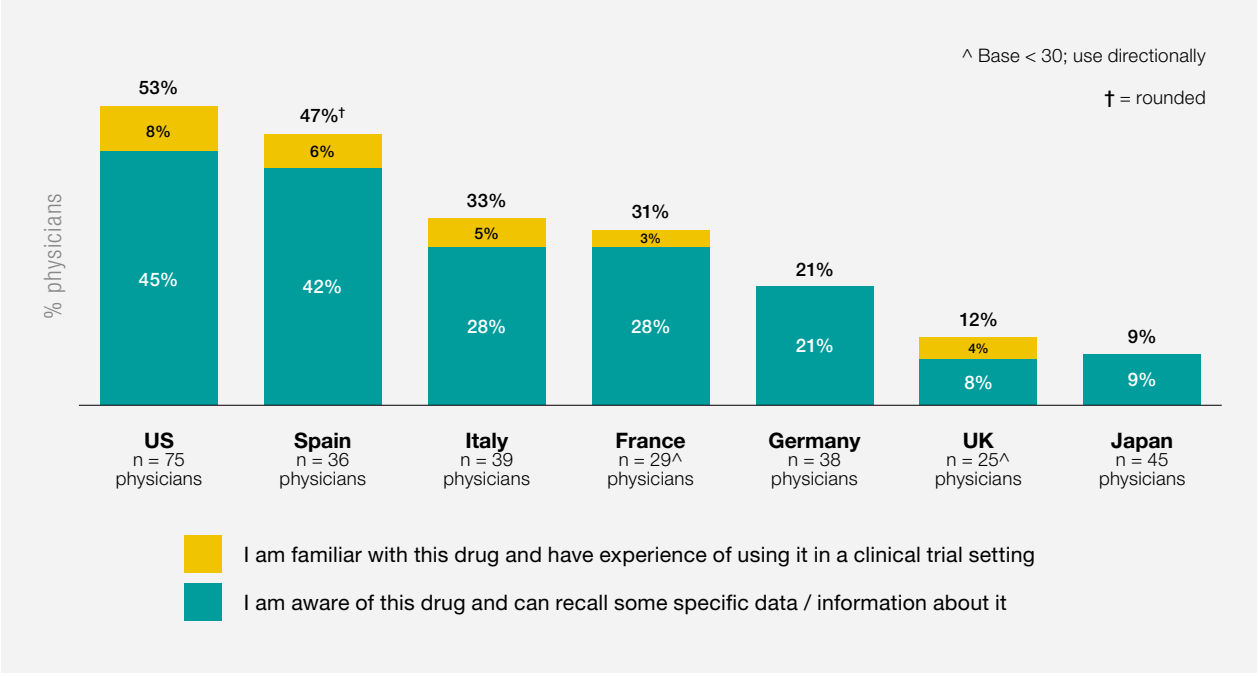


Source: Ipsos Haemophilia Therapy Monitor (Dec 2021- Feb 2022, 167 physicians in EU4 + UK (equal split across countries) reporting on 5-7 haemophilia A patients and 1-2 haemophilia B patients, 45 physicians in Japan reporting on 3 haemophilia A patients and 3 haemophilia B patients. Participating physicians were primary treaters, spent a minimum amount of time in direct clinical practice, and saw a minimum number of haemophilia patients in the last six months). Data collected online. Data © Ipsos 2022, all rights reserved.
*Gene therapies include: valoctocogene roxaparvovec, dirloctocogene samoparvovec, etranacogene dezaparvovec, fidanacogene elaparvovec, giroctocogene fitelparvovec

Ipsos' data also suggest that awareness of and familiarity with gene therapies in development differs across countries. Higher awareness was typically seen among sampled HCPs in Italy, Spain and the US across several therapy areas included in our analysis. In data deriving from our Q4 2021 Haemophilia TM, the physicians in our US sample had the highest level of awareness of gene therapies in development (53%), followed by their counterparts in Spain and Italy (47% and 33%, respectively). [FIGURE 3]

A similar trend was seen in data deriving from our Q4 2021 ATTR-CM TM, where awareness levels of CRISPR-Cas9 were higher among cardiologists surveyed in US, Spain and Italy than those in the other countries studied. In our Amyloidosis Polyneuropathy (ATTR-PN) TM data from EU4 in Q3 2021, once again cardiologists surveyed in Spain and Italy had the highest levels of awareness.

Figure 3: Prompted awareness of gene therapy developmental products for haemophilia amongst sampled physicians



Source: Ipsos Haemophilia Therapy Monitor (Dec 2021- Feb 2022, 167 physicians in EU4 + UK (equal split across countries) reporting on 5-7 haemophilia A patients and 1-2 haemophilia B patients, 45 physicians in Japan, reporting on 3 haemophilia A patients and 3 haemophilia B patients, 75 physicians in US reporting on 5-10 haemophilia A patients and 1-3 haemophilia B patients. Participating physicians were primary treaters, spent a minimum amount of time in direct clinical practice, and saw a minimum number of haemophilia patients in the last six months). Data collected online. Data © Ipsos 2022, all rights reserved.
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At the other end of the scale, only 9% of the physicians in Japan participating in our Q4 2021 Haemophilia TM were aware of and familiar with gene therapies in development – compared to 30% of physicians surveyed in EU4 + UK and 53% in the US. Of course, this lower awareness in Japan could in part be driven by lower prevalence of haemophilia in Japan compared to many of the major European markets[3].

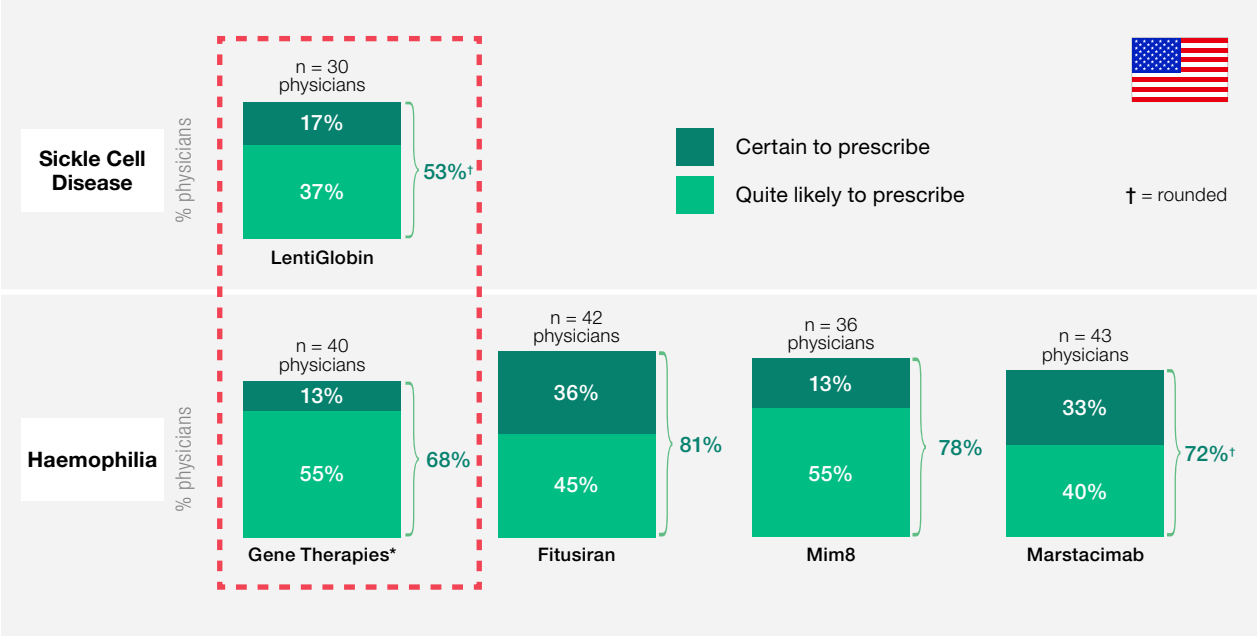
There may be multiple factors causing this higher awareness among HCPs surveyed in Italy, Spain and the US, one of which could be the level of investment and prioritisation by these countries into research and development of gene therapies. In Italy, for example, Sofinnova Partners (a venture capital firm) made a €6M investment in 2021 in three Italian gene therapy companies, cementing Italy's reputation as a European centre for cell and gene therapies[4]. Also in 2021, the Spanish government launched an initiative called the Strategic Projects for Economic Recovery and Transformation for Vanguard Health, a key objective of which is to position Spain as a leading country in the innovation and development of advanced therapies[5]. Further to this, data from the Alliance for Regenerative Medicine showed that cell and gene therapy funding growth between 2020 and 2021 was primarily driven by US developers[6].

Future use of gene therapies

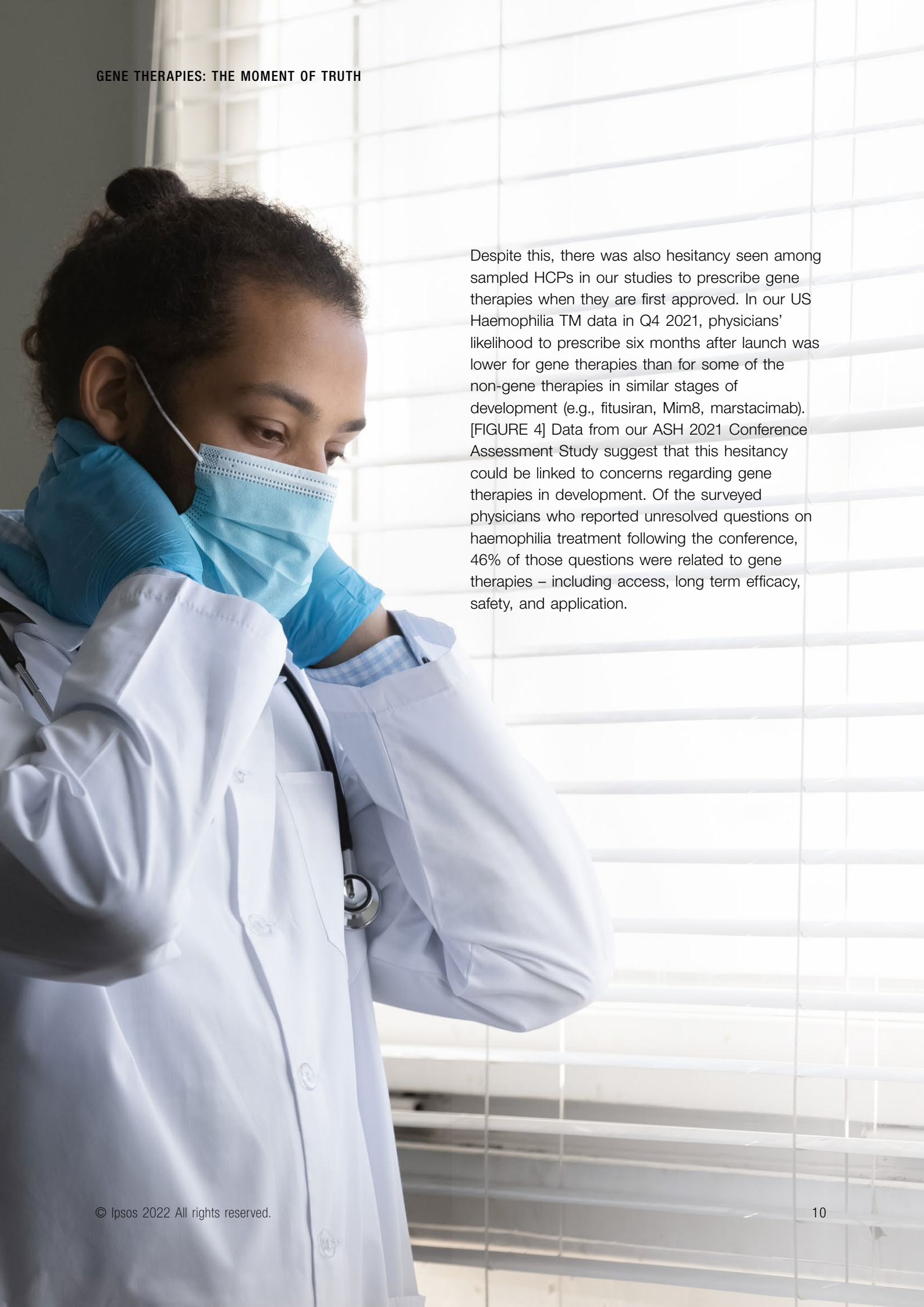
On the future of gene therapies, there is good news from our data. Of the US physicians in our Sickle Cell Disease and Haemophilia TMs who could recall data on developmental drugs, or had used them in a clinical setting, over 1 in 2 stated they would be likely to prescribe gene therapies in development for SCD within six months of launch (53%; LentiGlobin, specifically) and over 2 in 3 stated the same for haemophilia (68%). This is assuming the product is fully approved and there are no barriers to use. [FIGURE 4]

There was also an understanding of the importance of new gene therapies. 50% of EU4 & UK ophthalmologists / retinal specialists in our Q4 2021 Ophthalmology TM believed that gene therapies are important for the future of nAMD (rating 6/7 on 1-7 scale rating). In addition, a proportion of HCPs taking part in our syndicated Conference Assessment Studies cited gene therapies as the most interesting drug / developmental product based on what they had learned at relevant therapy area conferences. Specifically, 19% of HCPs cited gene therapies as the most interesting haemophilia developmental product at the ISTH 2021 virtual congress (EU4 & UK / US participants, n=91) and at the ASH 2021 Annual Meeting (EU4 & UK / US / Japan participants, n=70). Meanwhile, 17% cited gene therapies as the most interesting SCD developmental product at ISTH 2021 (EU4 & UK / US participants, n=98).

Figure 4: Sampled physician stated likelihood to prescribe current developmental products six months post launch



Source: Ipsos Sickle Cell Disease Therapy Monitor (Nov-Dec 2021, 74 physicians in US reporting on 629 patients seen in consultation. Participating physicians were primary treaters and saw a minimum number of SCD patients in the last six months). Ipsos Haemophilia Therapy Monitor (Dec 2021- Feb 2022, 75 physicians in US reporting on 5-10 haemophilia A patients and 1-3 haemophilia B patients. Participating physicians were primary treaters, spent a minimum amount of time in direct clinical practice, and saw a minimum number of haemophilia patients in the last six months). Data collected online. Data © Ipsos 2022, all rights reserved.
*Gene therapies include: valoctocogene roxaparvovec, dirloctocogene samoparvovec, etranacogene dezaparvovec, fidanacogene elaparvovec, giroctocogene fitelparvovec



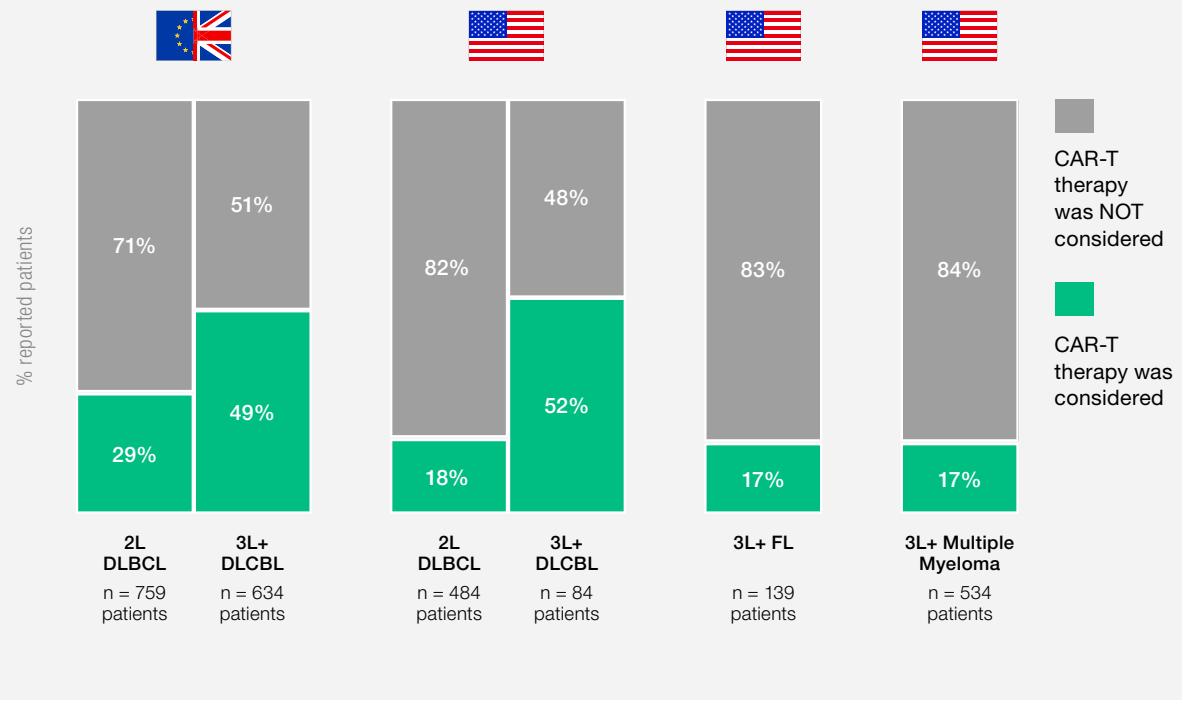
Despite this, there was also hesitancy seen among sampled HCPs in our studies to prescribe gene therapies when they are first approved. In our US Haemophilia TM data in Q4 2021, physicians' likelihood to prescribe six months after launch was lower for gene therapies than for some of the non-gene therapies in similar stages of development (e.g., fitusiran, Mim8, marstacimab). [FIGURE 4] Data from our ASH 2021 Conference Assessment Study suggest that this hesitancy could be linked to concerns regarding gene therapies in development. Of the surveyed physicians who reported unresolved questions on haemophilia treatment following the conference, 46% of those questions were related to gene therapies – including access, long term efficacy, safety, and application.

Insights from CAR-T cell therapy in oncology

Chimeric antigen receptor T- (CAR-T) cell therapy has been available for use in oncology since 2017, with the US launch of Yescarta for later line relapsed or refractory large B-cell lymphoma (DLBCL)[7]. Since then, CAR-Ts have expanded their label and launched into other oncology indications.

However, insights from our syndicated Global Oncology Monitor for the Q1 2022 moving annual total (MAT) time period reveal that CAR-T cell therapy is still not considered for a notable proportion of the DLBCL patients reported by sampled oncologists for which the label is approved. This is four years after launch of Yescarta. The oncologists surveyed would consider a CAR-T therapy for 49% and 52% of their reported 3rd line+ DLBCL patients, and for 29% and 18% of their 2nd line DLBCL patients in EU4 & UK and US, respectively. In addition, one year post launch of CAR-T therapies for follicular lymphoma (FL) and multiple myeloma (MM), only 17% of reported 3rd line+ patients were considered suitable for CAR-T treatment by US oncologists included in the study, underscoring a slow initial adoption at launch. [FIGURE 5]

Figure 5: Sampled oncologists' consideration of CAR-T therapy for reported oncology patients



Source: : Ipsos Global Oncology Monitor (Apr 21 – Mar 22), physicians in US and EU4 + UK (equal split across countries) reporting on specific quotas of DLCBL, FL and MM patients seen in consultation, data collected online. Participating physicians were primary treaters and saw a minimum number of patients per month. Sample data were projected to the wider clinical population). Data collected online. Data © Ipsos 2022, all rights reserved.

Meanwhile, data from our MAT Q1 2022 Global Oncology Monitor also suggest that patient refusal is a key barrier. 38% of reported 3rd line+ DLBCL US patients and 17% of reported 3rd line+ DLBCL EU4 & UK patients who were not considered a suitable recipient for CAR-T therapy were deemed so due to 'patient refusal' (as cited by sampled oncologists). In reported FL and MM 3rd line+ patients who were not considered for CAR-T therapy, patient refusal was mentioned for 20% of the records collected. Given that both oncologists and patients have had a few years to become familiar with CAR-T treatments, this data suggest that more needs to be done to encourage usage of these therapies.

Consumers' questions about gene therapies

As noise around any novel therapy grows, so too do questions from the general public – on everything from mode of action to efficacy to ethics. Gene therapies are no exception.

To see the types of question being asked about "gene therapies" online, we did a quick pulse via search listening tool, 'Answer the public'[8]. While most of the questions sought information about what gene therapies are and how they work, there were also questions related to approvals, and searches including the term 'cancer'. There were also a number of questions, indicating terms which are more common and trending, that were linked to more negative sentiment (see those in FIGURE 6 with darker green dots), including 'disadvantages of gene therapy to society', 'disadvantages of using gene therapy', 'why are gene therapies so expensive?' and 'why is gene therapy illegal / bad?'. This suggests that public perception of gene therapies varies in awareness, knowledge and acceptance. [FIGURE 6]

Figure 6: Consumer search questions for gene therapies

Source: Answer the public - Location set to UK, search term "gene therapies"

A role for industry to bridge the knowledge gap

Data from the referenced Ipsos studies reveal that while there is a buzz and interest about gene therapies among our sampled HCPs, there are also varying levels of awareness of gene therapies in development, and some reluctance by the HCPs to use these products upon launch. This could be driven by limited HCP knowledge and experience with these therapies, and whether they actively seek to learn information about new products, for example, by attending conferences.

This raises opportunities for pharmaceutical companies to provide more stakeholder education regarding gene therapies in development, to better inform HCPs and ensure they are armed with sufficient knowledge to provide adequate advice to patients when these products become available. This education should not be limited to developmental products, however, as learnings from the Global Oncology Monitor on CAR-T cell therapies show that stakeholder education and outreach is still required for marketed products.

We believe it is also important for companies to provide patient-friendly information to the public to bridge the gap between scientific advance and lack of understanding of this progress among patients. Furthermore, this will build advocacy and understanding among stakeholders prior to launch, at a time where there may also be market access (affordability and accessibility) challenges which could impact the success of these gene therapies. In our opinion, this investment will help to ensure HCPs and patients are committed to fully embrace gene therapies in the future.

About the Research

The Ipsos Haemophilia Therapy Monitor is a physician-reported syndicated patient record database, capturing prescribing of treatment for haemophilia A and B patients. Participating physicians are screened for specialty, time spent in clinical practice, number of haemophilia patients seen in the last six months and must be the primary decision-maker for their patients. Each wave, participants provide demographic information, de-identified information on a quota of haemophilia A and B patients seen in consultation, and responses to a perceptual questionnaire. Data used in this article were collected online. Sample sizes are provided alongside the relevant charts.

The Ipsos Sickle Cell Disease (SCD) Therapy Monitor is a physician-reported syndicated patient record database, capturing prescribing of treatment for sickle cell disease (SCD) patients. Participating physicians are screened for specialty, number of SCD patients seen in the last six months and must be the primary decision-maker for their patients. Each wave, participants provide demographic information, de-identified information on a quota of SCD patients seen in consultation, and responses to a perceptual questionnaire. Data used in this article were collected online. Sample sizes are provided alongside the relevant charts.

The Ipsos Ophthalmology Therapy Monitor is a physician-reported syndicated patient record database, capturing prescribing of treatment for neovascular age-related macular degeneration (nAMD), retinal vein occlusion (RVO) and diabetic macular edema (DME) patients. Participating physicians are screened for specialty, number of patients seen in the last three months and must be the primary decision-maker for their patients. Each wave, participants provide demographic information, de-identified information on a quota of nAMD, RVO and DME patients seen in consultation, and responses to a perceptual questionnaire. Data used in this article were collected online. Data used in this article were provided by 253 ophthalmologists / retinal specialists in EU4 + UK, reporting on 3852 patients (1800 nAMD, 1517 DME, 535 RVO patients) seen in consultation between October - December 2021.

The Ipsos Transthyretin Amyloid Cardiomyopathy (ATTR-CM) Therapy Monitor is a physician-reported syndicated patient record database, capturing prescribing of treatment for ATTR-CM patients. Participating physicians are screened for specialty / board certification, number of ATTR-CM patients seen in the last month (US and EU4 + UK) / last six months (Japan) and must be the primary decision-maker for their patients. Each wave, participants provide demographic information, de-identified information on a quota of ATTR-CM patients seen in consultation, and responses to a perceptual questionnaire. Data used in this article were collected online. Data used in this article were provided by 560 cardiologists in EU4 + UK (n=209), US (n=311), Japan (n=40), reporting on 348 patients in EU4 + UK, 893 patients in US and 70 patients in Japan, seen in consultation between October - December 2021 (US), November - December 2021 (EU4 + UK, Japan).

The Ipsos Amyloidosis Polyneuropathy (ATTR-PN) Therapy Monitor is a physician-reported syndicated patient record database, capturing prescribing of treatment for ATTR-PN patients. Participating physicians are screened for specialty, number of ATTR-PN patients seen in the last six months and must be the primary decision-maker for their patients. Each wave, participants provide demographic information, de-identified information on a quota of ATTR-PN patients seen in consultation, and responses to a perceptual questionnaire. Data used in this article were collected online. Data used in this article were provided by 164 cardiologists in EU4 reporting on 510 patients seen in consultation between September - November 2021.

The Ipsos Global Oncology Monitor is a physician-reported syndicated patient record database, capturing prescribing of anti-cancer and supportive care agents. Participating physicians are screened for specialty, level of seniority and number of drug-treated cancer patients seen per study wave and must be the primary decision-maker for their patients. Each wave, participants provide demographic information and de-identified information on a predefined quota of oncology patients (across solid and liquid tumours) seen in consultation. Data used in this article were collected online. Sample patient data are projected to the wider clinical population. Sample sizes are provided alongside the relevant charts. The Global Oncology Monitor is validated with market sizing studies to ensure that the size and representativeness of the physician sample reflects the wider population of relevant treating physicians.

The Ipsos Syndicated ISTH 2021 Conference Assessment Study is a syndicated perceptual study gathering perspectives of attending physicians on their ISTH 2021 conference experience. Participating physicians were primary treaters and saw a minimum number of patients per month. Data were collected online. Data used in this article were provided by 104 physicians across EU4 + UK, US, and Japan.

The Ipsos Syndicated ASH 2021 Conference Assessment Study is a syndicated perceptual study gathering perspectives of attending physicians on their ASH 2021 conference experience. Participating physicians were primary treaters and saw a minimum number of patients per month. Data were collected online. Data used in this article were provided by 91 physicians across EU4 + UK, US, and Japan.

Definitions used

***Haemophilia gene therapies referred to:** Valoctocogene roxaparvovec, dirloctocogene samoparvovec , etranacogene dezaparvovec, fidanacogene elaparvovec , giroctocogene fitelparvovec. Awareness and likelihood to prescribe considers all five gene therapies. For example, sampled physicians' awareness of the gene therapy group is summarised by the total number of levels of knowledge of each gene therapy they are familiar with.

Awareness of developmental products: sampled physicians either can recall some specific data about the product or have stated experience of using the product in a clinical setting; awareness is prompted, unless otherwise stated.

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