



The development of this document was commissioned by the Cell and Gene Therapy Catapult. Funding was provided equally by the Cell and Gene Therapy Catapult, Gilead Sciences and Novartis.

Learning the lessons of today to deliver the treatments of tomorrow

Reflecting on NHS experience to date with CAR T – Thinkpiece 2.0

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Executive summary

In 2018, NHS England approved a chimeric antigen receptor t-cell therapy (CAR T) for patients with a rare form of leukaemia.¹ The first deal of its kind in Europe, this approval ushered in a new wave of precision medicine and positioned the NHS as a world-leader in the delivery of CAR T. The treatment was approved across Wales and Scotland in the following year with three therapies now available across the UK and more on the way.

In 2020, Kite, a Gilead Sciences company that manufactures CAR T, undertook a series of interviews with experts from across the NHS with first-hand experience of delivering CAR T therapies. These interviews informed a thinkpiece which would capture the early lessons of CAR T adoption and set out recommendations to ensure continued success.

Almost two years later, and with the ongoing expansion of CAR T therapies as well as a drastically altered environment with the continuation of COVID-19 and Brexit, it seems timely to revisit this piece of work and assess what has changed. This new thinkpiece has drawn on insights collated from interviewees across the NHS and supplemented by insights from Kite and Novartis, another CAR T manufacturer. A full list of those interviewed is included as an appendix.

This document outlines their perspectives on what the NHS has done well, and the challenges encountered. Although each interviewee offered unique insights into the delivery of CAR T, a number of recommendations were consistently highlighted as key to ensuring the NHS is ready for the growing wave of CAR T therapies and Advanced Therapy Medicinal Products (ATMPs) more generally. These include:

- **Increasing delivery capacity** - Horizon scanning to address infrastructure and estate planning challenges and find solutions must begin now, in advance of new products launching
- **Expanding the workforce** - Greater recruitment and training is needed to increase the workforce with provision made to expand levels of clinical expertise on CAR T delivery
- **Streamlining future service planning** - Work is needed to understand how best to streamline service planning as CAR T indications expand
- **Maintaining strong collaboration between the NHS and industry** - Successful expansion of CAR T delivery will be dependent on early engagement and consistent collaboration between manufacturers, the NHS, and CAR T delivery centres
- **Expanding the clinical trial environment** - Increased clinical trial funding with adequate staff resourcing and deployment are required to improve the clinical trial environment and reduce bottlenecks

- **Improving referral pathways** - Support for CAR T referral centres from the NHS, industry, and delivery centres is required to ensure consistent understanding of CAR T eligibility, driving equal access
- **Enabling early access** - The UK's early access schemes must be improved and fully funded to increase uptake and ensure new products reach all eligible patient populations as soon as they are available
- **Improving the patient experience** - Increased support for patients is required so that patients know what to expect and are supported throughout their treatment journey with holistic wrap-around care and allied services
- **Strengthening UK data sets** - Data collection and reporting must be improved to support clinical decision making and improve patient outcomes

Introduction

CAR T therapy is a specialist and advanced class of treatment that uses genetically engineered T-cells to recognise and target cancers. In patients who respond to treatment, CAR T offers the potential for long-term improvements.ⁱⁱ

This therapy class has been routinely available to patients in England for around three and a half years, with patients in Scotland and Wales having access since 2019.ⁱⁱⁱ Now delivered across fourteen specialist sites, the NHS' rapid adoption of these new personalised therapies has been impressive, demonstrating agility, ambition, and collaboration in overcoming the wide range of unique challenges these complex therapies present.

The 2021 Life Sciences Vision celebrated this success whilst demonstrating a drive to go further. Introducing the Vision, the Prime Minister, Boris Johnson, highlighted that through 'harnessing the transformative power of treatments such as cell and gene therapies, we can go further than ever before in meeting the economic, social, and moral imperative of levelling up world class health outcomes across the land.'^{iv}

The number of ATMPs coming to market over the next five years is expected to grow rapidly and span various disease areas.^v The Accelerated Access Collaborative predicted that between 2020 and 2023, 30 new ATMPs will undergo a National Institute for Health and Care Excellence (NICE) assessment.^{vi} Moreover, CAR T is only one of several ATMPs, which include gene therapy, somatic cell therapy, and tissue-engineered therapy, each of which offer the potential to transform patient outcomes and realise the ambitions set out by the Prime Minister.

These statistics demonstrate that despite the success in establishing CAR T therapies across the UK to date, these treatments are still in their infancy with their full potential in changing the way we approach and manage some of the hardest to treat cancers still to be met.^{vii} Despite this transformative potential, expanding these therapies will pose a number of significant challenges for the health service. CAR T therapies, and ATMPs more generally, are complex to administer, requiring hospitals to adapt

their ways of working, assemble large multi-disciplinary teams, and ensure their services meet heightened capacity requirements. It is therefore vital that the NHS begins preparations now to ensure the UK is ready for the future of ATMPs.

Responding to this evolution and to expand access to CAR T, NHS England is preparing to roll out a third wave of delivery centres. As this work begins, it's important that lessons from CAR T delivery to date are captured, reflected on, and incorporated. To support this, Kite, Novartis, and the Cell and Gene Therapy Catapult have undertaken a series of interviews with experts from across the UK to inform this thinkpiece.

The document sets out lessons and reflections captured during the interviews. It considers how the landscape is evolving, focusing on the many successes achieved thus far before considering the ongoing challenges. The final section puts forward reflections for the future. Whilst these reflections were captured in the context of CAR T, they may be applicable to other ATMPs and should be considered to help the NHS build on the enormous successes to date and scale up capacity now so that patients benefit from the newest ATMPs as soon as they come to market.

Lessons from the delivery of CAR T to date

The introduction of CAR T over three and a half years ago and subsequent roll-out of the wave 1 and 2 centres has had considerable implications for the health service and treatment of certain blood cancers. In order to inform the ongoing adoption of these therapies, and to support the roll-out of wave 3 centres, this section reflects on the thematic successes and challenges that have emerged in this time and should be factored into future planning.

Successes

Throughout the interviews, we were informed of a number of successes that have helped contribute to the impressive speed of CAR T adoption across the NHS. Specifically, we were made aware of the following:

1. The NHS remains agile and ambitious in its expansion of CAR T therapies

Since the launch of the first CAR T therapy, the NHS' rapid adoption and expansion of these treatments has been impressive. Interviewees attested to a complete culture shift from CAR T being an unknown entity to nationally high levels of clinical expertise and a strong network between industry and the NHS.

“There are a huge number of very dedicated people who have worked incredibly hard, overcoming enormous obstacles in the machinery of the NHS to quickly adopt and implement CAR T therapies”

Since CAR T's approval in late 2018, and the initial roll-out of wave 1 centres across nine sites in England and one in Wales,^{viii} three additional wave 2 sites have been added in England with a centre also created in Scotland.^{ix} Now constituting a national service, further expansion plans are underway with the creation of wave 3 centres and the possibility of a second centre in Edinburgh in addition to the Glasgow centre, where clinical trials are expected to commence from May 2022. Reflecting on this rapid expansion, there was confidence from many interviewees that the NHS has thus far responded to capacity challenges proactively and is taking steps to address constraints.

Clinicians interviewed noted that support from the NHS has been strong and consistent throughout the process of setting up delivery centres with service specifications being rapidly created to ensure treatments reach patients as early as possible. It was noted that the general patient pathways have improved and shortened, with referral to treatment times decreasing from an initial average of 72 days to just over 40 days.

It was felt that the UK is quick to launch CAR T products with the first approved CAR T being highlighted as receiving funding 10 days after licensing. The opportunity provided by NHS England for engagement prior to licensing was noted as key to facilitating early conversations about launch and access, ultimately expediting the process.

It remains clear from the success in establishing CAR T that the NHS can move quickly, decisively, and with real ambition. As the CAR T treatments multiply, spanning new disease areas, it will be crucial that the NHS retains this entrepreneurial spirit, so it can remain at the forefront of this treatment revolution.

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2. Collaboration between manufacturers and CAR T delivery centres remains exemplary

Collaboration between manufacturers, CAR T delivery centres, and the wider NHS network remain exemplary and has been another key determinant of the success of CAR T adoption.

Clinicians interviewed attested to good support from manufacturers throughout the delivery centre creation process and thereafter, stating that industry colleagues were easy to get hold of and regularly in touch. Additionally, the CARNet meetings, industry-run conferences for delivery centres, were deemed to be useful for sharing learnings.

“Engagement with industry has gone from strength to strength – communication starts earlier; onboarding has become simpler; and training more time efficient”

Interviewees believed that as CAR T treatments have expanded, collaboration has gone from strength to strength. It was noted that the industry onboarding processes have become more efficient as centres have onboarded additional products with documents from manufacturers becoming clearer and engagement beginning earlier. Shifts in manufacturer training models with the introduction of cascade training and train the trainer were identified by centres as being more manageable and time efficient.

Interviewees believed that this strong collaboration was invaluable in overcoming challenges presented by COVID-19 and Brexit and that closer communication to address these challenges and build robust contingency plans led to greater clarity of responsibility and new ways of working. Concerns were raised that with some ongoing uncertainty surrounding the impact of Brexit, it's important that this strong collaboration continues to ensure new challenges are quickly overcome and to support the NHS in maintaining its leading position in CAR T delivery.

3. The National Panel has continued to support CAR T delivery

Interviewees noted that CAR T National Panels have continued to be useful in supporting CAR T delivery and that they were particularly key in early roll-out. These clinical bodies were set up by NHS England with the responsibility for approving and prioritising access requests. In Scotland, a multi-disciplinary team (MDT) provides the same function.

Some interviewees commented that these organisations continue to ensure consistency of decision-making and help mitigate geographical inequalities whereby a patient's location may determine their access to treatment. In Scotland, clinicians noted that MDT attendance from a wide range of haemato-oncologists rather than just lymphoma leads was useful in spreading best-practice and improving CAR T education levels.

“The National Panel provided vital support in the early days of CAR T delivery, enabling a strong clinical network to share learnings, ensure consistency, and improve patient outcomes”

Although those interviewed recognised the value of the Panel to date, uncertainty was raised about its role going forward. It was felt that as the number of new centres grows and with the expansion of CAR T into earlier lines of treatment, a centralised National Panel may become unsustainable and may slow down patient referrals and impede patient access.

As wave 3 centres are brought onboard, it will be valuable to monitor this uncertainty and assess how to move forward. It was suggested that the National Panel could transition to a local or regional MDT structure to ensure the continuation of a robust clinical network that can advise on difficult cases, whilst moving away from the current structure whereby every single patient case is discussed. Such a structure would expedite the patient referral process and reduce bottlenecks in the system.

4. Support from wave 1 to wave 2 centres has been invaluable

Whilst establishing CAR T delivery remains complex, interviewees highlighted that strong support from wave 1 to wave 2 centres has considerably lessened this burden. Wave 1 centres have been proactive in sharing protocols and standard operating procedures (SOPs) and it was noted that centres in London, that see the largest number of patients, offer strong support to regional centres in managing rarer side-effects and toxicity.

“Centre to centre engagement and support is vital in successful CAR T delivery – we must not reinvent the wheel”

Consensus on the value of peer-to-peer support in establishing and managing CAR T delivery was strong but it was flagged that these support networks, which remain informal, may be inconsistent with clinicians commenting that they relied on personal relationships at other centres. Two interviewees noted that they had heard of plans to introduce a ‘buddy scheme’ for clinicians establishing wave 3 centres. Whilst this plan is still in its infancy, support for the idea was strong. Looking ahead to wave 3 centre roll-out, informal networks should be formalised to ensure lessons learnt and best practice from the establishment of earlier centres are shared.

5. Despite the challenges of COVID-19, the system reacted swiftly to mitigate disruption

The challenges of COVID-19 have been extensive with interviewees commenting that all day-to-day services were greatly altered. Interviewees reported increased time for funding approvals, a reduction in nursing staff with many moving to different areas or retiring, reduced staffing numbers due to isolation rules or contraction of COVID-19, and uncertainty about the impact of the disease on patients. It was also noted that COVID-19 had a considerable impact on the establishment of services with the opening of the delivery centre in Leeds being delayed by seven months.

Despite these challenges, all interviewees believed that the system pulled together, reacting swiftly to mitigate disruption. It was noted that CAR T patients were prioritised with almost all treatment continuing and centres recording little disruption. Only one centre reported delays to treatment for just one patient due to COVID-19; Scotland reported a consistent median time from MDT to transfusion of 54 days and no interruption to patients who needed intensive care. There were no reported delays in manufacturing.

“COVID-19 continues to circulate in our communities and CAR T patients remain extremely vulnerable; work must continue to protect patients and mitigate these risks”

It is evident that the system has adapted to the pandemic, improving efficiencies by reducing reliance on face-to-face contact, introducing flexibility into staff roles, and enhancing cross-centre collaboration. Interviewees commented that some of these efficiencies are here to stay and that whilst the risk of disruption was extensive, all stakeholders reacted swiftly to minimise this. With hindsight the protection

of CAR T services has been a success, once again highlighting the agility and dedication of all parties involved in CAR T delivery.

Challenges

Despite the numerous successes, the interviewees also identified a range of challenges which will need to be factored into NHS planning for the future rollout of CAR T. Specifically, we were made aware of the following:

1. Establishing CAR T delivery remains challenging

Although, as mentioned, the challenges in establishing CAR T delivery have diminished over time with its expansion across the UK and growing clinical expertise, interviewees were keen to highlight that it remains complex.

“CAR T therapy constitutes an entire service which must be tailored for a patient to make it as quick, efficient, and reliable as possible. Establishing such a service is challenging”

These challenges present across the pathway from approval and launch to the establishment of centres and delivery of treatment. Regarding approval and launch, interviewees noted that clearer communication is sometimes needed on where industry can engage with the NHS.

At a UK-wide level, concerns were raised that whilst launch is quick, progress can be slow, hindered by the inability to begin preparatory service development until product approval. It was noted that from final appraisal determination it takes around three months to deliver the product to a patient.

We also heard concerns regarding the considerable gap between NICE approval and Scottish Medicines Consortium (SMC) approval of lymphoma CAR T treatments meaning that some Scottish patients have had to be treated via Peer Approved Clinical System requests. These have been funded by health boards which has posed challenges in terms of securing funding and service provision given a service cannot be funded for a new CAR T until it has been SMC approved.

Regarding the establishment of centres, interviewees highlighted challenges in gaining Joint Accreditation Committee ISCT-Europe and EMBT (JACIE) accreditation, getting approval from the NHS, understanding and meeting NHS evidence requirements, and managing the large number of SOPs required by industry.

Workforce capacity constraints were cited as leading to delays in establishing centres, with clinicians noting the need for strong administrative teams comprised of business managers, data coordinators, and quality managers to support this process. Many of these roles exist for transplant centres, easing the process, but for other centres establishing these diverse teams remains challenging.

Those interviewed acknowledged that the personalised nature of CAR T means its delivery will always be challenging but they believe the obstacles highlighted above may be overcome with improved communication, planning, and resourcing. As more products launch and wave 3 centres begin their

roll-out, it's an important time to look at the end-to-end process to identify bottlenecks and consider how they may be overcome.

2. Variation in treatment and access persists across the UK

We heard that variation continues to exist between the centres, particularly in relation to the number of patients treated. Interviewees recalled an earlier belief that as CAR T expansion progressed, this variation would naturally diminish but it appears that although the treatments are now available nationally, variation continues.

“There is still variation in access, not all eligible patients have the same access to CAR T treatments”

We heard reference to London's delivery centres seeing the largest number of patients and thus having the greatest clinical expertise, particularly in managing side-effects. Variation in the delivery of post-transplant care was also raised with concerns that CAR T delivery centres and hospitals were not always clear about where responsibilities for patient care lie.

Variation was also flagged in the referral pathways. In England it was noted that some referral centres have never referred patients for CAR T. Across Scotland and Wales challenges regarding access were highlighted due to the existence of only one centre in each country which poses geographical barriers meaning some patients and their families are required to travel a long way for treatment which can be an additional burden.

Looking ahead, strong collaboration between the centres, as well as education for referral centres, is key to reducing this variation. This is important not just for increasing the number of patients who are treated with CAR T but also for ensuring that the centres grow in confidence using ATMPs, which should enable future therapies to be more readily adopted into routine care. It was also recommended that further work is undertaken to understand the gap in referrals and ensure adequate support for all centres.

3. Physical infrastructure and estate planning challenges hinder expansion of CAR T

Interviewees remained concerned about a number of physical infrastructure challenges that will, if left unaddressed, hinder the expansion of CAR T. Individuals cited capacity challenges relating to cold-storage units, apheresis, intensive care unit, cell labs, and bed space.

In particular, the apheresis capacity challenges were highlighted by a number of interviewees with many citing this as the single largest barrier to the future expansion of CAR T. We spoke to a clinician who, due to lack of onsite facilities, outsourced their apheresis services to NHS Blood and Transplant (NHS BT). Whilst overcoming the on-site capacity challenges, the complexity of working with another provider was flagged as adding additional difficulties to the pathway. It is predicted that six out of the 10 new centres will utilise the NHS BT services for apheresis.

“There are capacity challenges at every level of the NHS with regards to CAR T delivery. With a pipeline of new indications coming along these capacity challenges will prevent patients from accessing treatments”

Additional challenges relating to post-infusion capacity were raised with concerns that there is not always adequate space for patients to remain in hospital post-infusion and receive the care they need. Clinicians also noted infrastructure challenges regarding the outpatient service for those patients well enough go home post day 14 who will require considerable outpatient support including suitable accommodation and transport. This lack of outpatient provision means some patients stay on the ward unnecessarily, compounding capacity constraints.

There was consensus amongst interviewees that more centres must open to deliver commissioned services and the full range of clinical trials. It is also vital that these centres are set up or redesigned to meet safety obligations and avoid possible delays in the future. It's important that these capacity constraints are addressed now, to keep pace with the extensive CAR T pipeline and growing patient numbers.

4. Workforce challenges remain

Interviewees unanimously cited workforce constraints as challenges in the environment now and a barrier to future expansion. It was again noted that the complexity of the teams required to deliver CAR T therapy including specialists from immunotherapy, ITU, nursing, psychology, neurology, pharmacy, and laboratory can be hard to bring together and make it difficult to scale up access. Shortages on the administrative side concerning data and quality managers, and business administrators and coordinators were flagged. Perhaps reflecting a greater understanding of how CAR T impacts patients, the interviewees also raised concerns regarding the number of allied staff needed including dieticians, and psychological support.

“The current workforce is stretched and demands will only increase over the next few years”

To prepare the environment for more CAR T indications, it's important these workforce capacities are addressed with the correct teams established early on. Services need the necessary supporting infrastructure and specialist staffing capacity to meet JACIE standards, and this should be considered as part of the national planning process for the third wave.

5. The clinical trial landscape can be slow and difficult to navigate

Perhaps reflecting the considerable wave of innovation in CAR T treatments, and ATMPs more generally, interviewees were keen to discuss challenges in the clinical trial environment.

The group stressed that the UK has good experience in delivering clinical trials with a strong network of sites and largely successful recruitment, once trials are set up. Approximately 9% of all ongoing ATMP trials are currently conducted in the UK, demonstrating the appeal of the country for ATMP clinical development.^x Despite this statistic we heard from manufacturers that the UK clinical trial landscape is viewed internationally as expensive and challenging; sign-off procedures are complex, deadlines are missed, and establishing trials is arduous. It was noted that CAR T clinical trials were

impacted during COVID with nursing staff being removed from trials and COVID-19 trials being prioritised.

“The UK clinical trial scene is viewed internationally as expensive, challenging, and slow”

Interviewees noted examples of some countries having set up and recruited patients to their trials long before the UK, meaning these countries are given preference for future studies. France, Germany, Italy, and Switzerland were cited as being efficient with the U.S., whilst expensive, also highlighted as a leader in this space. It was concluded that the UK clinical trial environment, whilst not bad, must not rest on its laurels and must strive to become more efficient and competitive in attracting the best trials.

Reflections for the future

In discussing the challenges and successes of CAR T delivery to date, interviewees also reflected on the future of CAR T. These reflections were based around a broad consensus that the number of CAR T products, and ATMPs more generally, will grow over the coming decade and are likely to span into solid tumour cancers and even possibly other disease areas.

It was unanimously felt that this shifting landscape will compound the challenges set out above and that as such, to prepare for this future, the NHS must begin planning to implement service changes to meet the increased capacity requirements these new therapies will require. In particular it was felt that:

Horizon planning to address infrastructure and estate planning challenges must begin now

There was unanimous concern that infrastructure challenges, if left unaddressed, will mean the NHS is ill-equipped to provide the increased number of CAR T therapies expected over the coming years. It was felt that to manage this challenge, planning must begin now, informed through enhanced horizon scanning, and will require strong collaboration between industry, centres, the NHS, and the Cell and Gene Therapy Catapult. It was noted that through horizon scanning, CAR T myeloma indications have already been identified as likely challenging for existing capacity given the higher prevalence of patients with multiple myeloma compared to existing CAR T indications. Despite this insight, there has thus far been little proactive support to increase capacity to the required levels within the existing centres.

“Additional centres must be qualified ahead of indication launches so they can provide the most innovative treatments as soon as they become available”

Interviewees agreed that the current number of 14 CAR T delivery centres across the UK will be insufficient to meet heightened demand and welcomed plans by NHS England to expand the number of centres further. It was also noted that in Scotland and Wales, with only one centre each, a strategy must be adopted to support the development of additional sites in advance of new products launching. In Scotland, as mentioned above, the viability of formally commissioning a second centre is being considered as part of a national review. It is noted that a second Scottish centre is currently awaiting the outcome of a JACIE inspection which may accredit the service to provide CAR T cell therapy. In

Wales, with only one allogeneic centre and no other centres having the infrastructure to meet JACIE standards, responding to this challenge will be harder.

Some interviewees suggested that to increase capacity, the NHS could consider creating purpose-built cellular therapy units or begin onboarding every allogeneic centre to become a CAR T centre, with the same option possible for autograft centres. It was noted that as hospitals are built, provision for CAR T storage facilities should be considered and the NHS and industry must work closely together to develop alternative and increased storage, supply chain, product movement options, and apheresis capacity. The possibility to use industry infrastructure to store products until the exact time they are needed by centres was also suggested. It was noted by manufacturers that capacity challenges across industry must be addressed too, with steps already being taken to ramp up manufacturing capacity and facilities.

The possibility of CAR T treatments being delivered in an ambulatory setting was also highlighted as a strategy to address capacity challenges in future with one centre having already written their ambulatory care pathways. Although it was noted that ambulatory delivery is still some way off and will be dependent on safety considerations and only appropriate for patients with lower-grade disease, it holds exciting potential to transform care pathways and reduce capacity challenges.

Workforce capacity constraints must be addressed

It was noted by interviewees that addressing infrastructure constraints is only half the challenge and must be supported by growing the workforce and enhancing levels of expertise. The group agreed that increased staff recruitment must be prioritised with training programmes implemented to upskill clinicians on CAR T delivery. Increased training funding will be required and greater flexibility to provide remote training will make it more accessible to clinicians and reduce capacity challenges.

“To ensure the centres are ready, increased staff recruitment must be prioritised and education programmes should be implemented to upskill existing clinicians to successfully deliver treatment”

Concerns were raised that as the CAR T pipeline expands, the burden on clinicians will become unmanageable. To mitigate this challenge, interviewees suggested industry streamline their product training packages. Whilst acknowledging the granularity required to meet regulatory and licensing requirements, it was suggested that steps could be taken to standardise the onboarding process, highlighting commonalities across indications to make them applicable for a wider range of products and reduce time burden. Interviewees advised that cooperation at an industry level would be required to make this happen with some sort of centralised national direction to set national standards and key quality indicators across training programmes to mitigate the risk of variation in care emerging as product delivery expands.

Interviewees were keen to consider how to address workforce capacity requirements following the expected evolution of CAR T treatments into diverse therapy areas. It was noted that this expansion could be managed by increasing the number of haematologists and by upskilling general oncologists to deliver CAR T. The upskilling of pharmacy colleagues who will have a huge role to play in governance and management for CAR T patients will also be important. It was recommended this upskilling begin in advance of new product launches with haematology and oncology teams beginning now to work more closely. The development of an integrated cellular therapy network across hospitals to share best practice was suggested as a way to facilitate this collaboration. It was also proposed that,

eventually, the establishment of integrated cellular therapy units in hospitals would prevent silos and enable cross-therapy teams to deliver CAR T side by side and learn from one another.

Future service planning should be streamlined

Mirroring recommendations to streamline training, the interviewees also suggested that future service planning could be streamlined to ease the expansion of services. It was suggested that as more indications launch, the development of a standardised delivery template could expedite the adoption of CAR T indications. Some interviewees suggested that the establishment of a standardised information portal with template SOPs would make it easier to create service level agreements.

Alternative ideas to streamline service planning included beginning service delivery as early as possible so it runs in parallel with the appraisals process thus ensuring everything is in place to deliver treatments as soon as they are approved. Industry members noted that whilst manufacturers' main focus is, and will remain, the health technology assessment process, there is more they could do such as pathway mapping to support smooth service planning at an early stage. It was also suggested that service planning could be expedited if an individual in each of the centres was given sole responsibility for service planning.

Improving efficiencies in contracting was also flagged as key to simplifying service planning. It was suggested that each centre should have designated contract signatories and that the centralisation of contracting could also expedite the CAR T roll-out process. It was noted that in the context of the launch of Kite's second CAR T therapy, contracting documents from the first product were amended to enable them to be future proofed for forthcoming new CAR T indications, which greatly eased the process going forward.

Collaboration with manufacturers must be maintained

“Strong and early collaboration and cooperation between industry, clinicians, and centres is the keystone to successful delivery”

As discussed above, the strong collaboration between manufacturers, CAR T delivery centres, and the NHS is seen as a keystone of the successful adoption of CAR T. Whilst keen to highlight this success, interviewees also stressed that there were areas for improvement, particularly to ensure readiness for the expected wave of CAR T therapies in the next decade.

It was noted that in setting up new CAR T delivery centres, it is important that this collaboration begins as early as possible and that industry provides as much information up front, including greater clarity on the service impact, to support in improved service planning. It was suggested by one interviewee that a cross industry working group, such as the ABPI, might be well placed to lead on this collaboration.

“As more and more products become available, consideration should be made for how we streamline and simplify the onboarding process”

Regarding input from the centres themselves, interviewees suggested that having a named individual in each centre who was accountable for engaging with industry representatives, overseeing centre development, leading the onboarding process, and signing contracts would also improve the process.

As the CAR T pipeline expands and new ATMP manufacturers emerge, taking these steps to encourage strong collaboration from the outset will help ensure success in an increasingly crowded landscape.

The UK clinical trial environment must be expanded

Reflecting concerns surrounding efficiencies across the UK's clinical trial landscape, interviewees were keen to set out areas for improvement. Requests for increased clinical trial funding were voiced by a range of interviewees, along with adequate clinical trial staff resourcing and the proposition that individuals, dedicated to clinical trial research without clinical responsibilities, are employed to run the trials. It was also stressed that an adequate number of patients must be secured to partake in trials and that consistent communication between industry and trial sites is maintained with clear deadlines for reporting set out and met. This resourcing and funding must be in addition to the resources needed to deliver the commissioned service so that investment for clinical trials is ring-fenced to guarantee and optimise their delivery.

Interviewees were keen to stress the value of clinical trials. It was noted that trials offer hope to patients, who may have exhausted all other options, and contribute to improving clinical expertise. Additional benefits of encouraging clinical research in the NHS included the added benefits of preparing the landscape for product launches, strengthening the UK life sciences sector, and ensuring UK care pathways are represented in international research, were also put forward.

“Clinical trials must be prioritised. It’s easy to forget the human element associated with trials but positive trial outcomes pave the way for lives being saved and deliver real patient benefits”

Data shows that CAR T clinical trials in the UK are increasing year on year with 168 ongoing trials observed in 2021.^{xi} To continue this trajectory, it is imperative that the value of clinical trials in driving real improvements for patients is understood and the landscape adequately resourced.

“Ongoing education is required so that CAR T is not viewed as a treatment of the future but as a treatment available for all eligible patients today”

Improvements across the pathway must be strengthened to drive equal access

Regarding concerns about inequity of access to CAR T, as well as suggesting improved communication between centres as set out in the previous section, interviewees also pointed to the importance of improving referral pathways. It was recommended that the NHS and industry, alongside the treatment centres, work collaboratively to enhance understanding of CAR T eligibility amongst referral sites. It was also stressed that messaging to referral centres must look to upskill on the optimal time in the treatment pathway to refer to CAR T to avoid overtreatment with earlier lines of therapy. To aid in this educational piece, interviewees highlighted the importance of educating a range of roles in addition to referring clinicians including GPs and pharmacists so that the clinical workforce, as a whole, is better equipped to put eligible patients forward.

It was noted that there also existed an opportunity to improve the UK's various early access schemes to support equitable access and uptake with interviewees suggesting that the UK could learn from international comparisons. France was lauded as leading the way with several fully funded schemes

that enable patients to access new treatments earlier, ensuring clinicians remain at the cutting edge of new ATMP technologies. With upcoming CAR T products targeting both larger patient populations but also those with rarer diseases, these early access schemes will be ever more important in enabling equal access.

Driving access is also dependent on robust appraisal and reimbursement systems that accurately value innovative new medicines. The recent NICE review of its methods and processes provided the opportunity to improve these systems. Whilst some changes were implemented, concerns have been raised that they did not go far enough and NICE should explore further updates to support access to cell and gene therapies through its iterative review process without any delay.

Improvements in education and patient experience should be made

Delivering improvements in patient experience and listening to the patient voice were raised. This growing focus perhaps reflects a greater understanding of the impact of CAR T on patients. Interviewees noted that education around CAR T therapy, the likely patient experience and challenges commonly faced, should be improved to better equip individuals before treatment. Clinicians highlighted the need to better manage patient expectations and to understand what matters to them as they embark on their treatment journey.

“More funding for allied care professionals including dietitians, physiotherapists, mental health specialists, and palliative care teams is required to provide the holistic care that patients need”

Interviewees highlighted the need to provide wrap-around care and better support networks. It was noted that improvements across allied patient services, including greater provision of dietitians, physiotherapists, onco-psychologists, palliative teams, and fertility experts, were needed to make this happen.

To support better patient care, interviewees also noted a need to collect more meaningful data to better understand the patient experience and how pathways can be altered to improve this. The need to include this data in the appraisals process with greater weight given to quality of life was also noted as being important to enabling a more accurate understanding of the impact of these technologies.

UK data collection methods and datasets must be strengthened

In continuing to enhance clinical understanding of CAR T and secure the best outcomes for eligible patients it was noted that the UK must focus on ameliorating data sets. Interviewees praised the UK's robust CAR T data collection but noted that it relies on a small number of individuals giving up a great deal of their time to manage it. Increased funding is required to support the establishment of a more formalised registry that would support improved clinical decision making.

“As CAR T products multiply, it's vital our data collection expands, becoming increasingly robust and granular to support knowledge growth and improved decision making”

France was cited again as providing best practice in this area with DESCAR T, and the registry for diffuse large B-cell lymphoma (DLBCL) being applauded for its granularity and reliability. In supporting the future expansion of CAR T therapies, it is important the UK's data sets are improved to equip decision-makers with the information they need to inform patient care and pathway alterations.

Conclusion

NHS adoption of CAR T delivery has been impressive. All interviewees stressed the enormous ambition and dedication of so many individuals who have worked tirelessly to facilitate this adoption, taking the NHS from a standing-start to a world leader in the delivery of CAR T in a very short space of time. This enormous achievement demonstrates that with continued ambition the NHS can prepare itself to facilitate the predicted expansion of CAR T therapies and ATMPs over the next decade.

However, the magnitude of this task must not be underestimated. Perhaps most importantly, preparation work and horizon scanning must begin now. It's vital that all stakeholders come together to ensure continued collaboration, planning, and preparatory work so that the potential barriers impeding the uptake of the latest therapies can be overcome. This will ensure the system is fully prepared to enable NHS patients to continue to benefit from the latest innovations as soon as they launch.

Appendix: interviews conducted

This document has been informed by interviews with the following individuals:

Dr Anne-Louise Latif, Queen Elizabeth University Hospital
Dr Craig Wheelans, National Medical Advisor for Specialist Healthcare Commissioning and National Networks
Denise Calder, General Manager, Cancer Services, NHS Lothian
Dr Frances Seymour, Leeds Teaching Hospitals Trust
Letty Hanning-Lee, Gilead
Ed Jenkins, Novartis
Liza Loidolt, Gilead
Michelle Murchie, Novartis
Dr Keith Wilson, Cardiff and Vale UHB

ⁱ NHS, [NHS England strikes deal for ground breaking cancer treatment in a new European first](#), 5 October 2018

ⁱⁱ The Guardian, [First patients of pioneering CAR T-cell therapy 'cured of cancer'](#), February 2022

ⁱⁱⁱ NHS, [NHS England strikes deal for ground breaking cancer treatment in a new European first](#), 5 October 2018; Cancer Research UK, [CAR T cell immunotherapy now available through NHS Scotland for some adults with lymphoma](#), September 2019; The Pharmaceutical Journal, [First patient in Wales to begin CAR-T personalised therapy](#), November 2019

^{iv} HM Government, [Life Sciences Vision](#), 2021

^v PharmaTimes, [UK sees a 20% growth in the number of advanced therapy trials, report finds](#), February 2021; Accelerated Access Collaborative, [Advanced Therapy Medicinal Products \(ATMPs\)](#), 2020

^{vi} Accelerated Access Collaborative, [Advanced Therapy Medicinal Products \(ATMPs\)](#), 2020

^{vii} The Guardian, [First patients of pioneering CAR T-cell therapy 'cured of cancer'](#), February 2022

^{viii} NHS England, [Implementing CAR T cell therapy in the NHS](#), May 2019

^{ix} University Hospital Bristol, [How to get lymphoma patients to CAR-T therapy in the UK](#), June 2019; CRUK, [CAR T cell immunotherapy now available through NHS Scotland for some adults with lymphoma](#), September 2019

^x The Cell and Gene Therapy Catapult, [The Cell and Gene Therapy Catapult UK clinical trials database](#)

^{xi} The Cell and Gene Therapy Catapult, [The Cell and Gene Therapy Catapult UK clinical trials database](#)