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Horizon Scan of the Artificial Blood Research and Funding Landscape

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Key findings

- Eleven clinical trials were identified relating to artificial blood products. Of these, the trial status for five was terminated or unknown, three were recruiting or not yet recruiting and three completed. No study results were published.
- Four trials were sponsored by industry and seven by other sponsors, such as universities, healthcare organisations and individual researchers.
- The highest number of trials was carried out in France and the USA (three each), followed by the UK and Hong Kong (two), then New Zealand (one).
- Six technologies were identified across these trials with HEMO2life being the most investigated (four trials)
- Our funding scan identified nine non-NIHR projects worldwide, with the majority being in the UK. The largest proportion of total funding spend (£2.1 million) was from the Wellcome Trust across two projects. However, most projects (five) were funded by the National Institute of Health (NIH) in the USA.
- In the published literature, including preclinical studies, haemoglobin-based oxygen carriers were most prevalent, with most research happening in the USA, China, Europe, Canada, and Japan. Two technologies (PolyHb and VS-101) are in preclinical studies only; five other technologies (HemAssist, PolyHeme, Hemolink, Hemospan, and Hemoximer) have been discontinued.

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Current literature

Locations performing the most research in this field:

- USA
- China
- Europe
- Canada
- Japan

Haemoglobin-based oxygen carriers were the most investigated

Some technologies:

- Are only in pre-clinical studies
- Have been discontinued

Trial data

11 clinical trials worldwide

Study Locations

3 France | 3 USA | 2 UK | 2 Hong Kong | 1 New Zealand

4/11 trials for HEMO2life®

6 different technologies identified

No results currently available

5 trial status unknown/terminated

3 recruiting/not yet recruiting

3 Completed

Funding

£2.1M from the Wellcome Trust across 2 projects

9 Non-NIHR projects worldwide (most in the UK)

45.5% National Institute of Health (NIH) provided 45.5% of project funding, making it the top funder.

Background

What is artificial blood and how is it used?

We have focused on artificial blood or blood products used to support transport of oxygen around the body. We have not considered other methods used to support blood volume only.

There are two major types of oxygen therapeutics: haemoglobin (Hb)-based oxygen carriers (HBOCs) and perfluorocarbon-based oxygen carriers.[1] The Hb for most HBOC products is derived from expired human blood, fresh bovine (cow) or porcine (pig) blood, and some marine invertebrates. The production of HBOCs involves the chemical modification of harvested Hb using methods including polymerization (creating Hb chains), cross-linking Hb tetramers (Hb molecules consist of four sub-units in total (two α-subunits and two β -subunits) – meaning they are tetramers) or encapsulating Hb within membranes that mimic the environment present within red blood cells (RBCs). These methods are used to reduce toxicity that can lead to adverse effects in artificial blood recipients and prolong the half-life of the Hb.[2]

Methods

Literature searches

Searches for trial records were conducted on the Clinicaltrials.gov trial registry and the Innovation Observatory's ScanMedicine trial portal on 24th April 2024, using a range of terminology relating to artificial blood either generally or for specific products. Searches for funding data were conducted on a range of funding platforms (see appendix for details). A targeted search for reviews plus a more specific and limited search of non-review articles was conducted on Ovid Embase. A date limit of 2019 onwards was applied across all searches (trial completion date, funding end date, review/article publication date). See appendix for full details of all searches.

Eligibility criterion

The eligibility criterion was any product that aimed to perform a key function of blood, namely the transportation of oxygen around the body.

Record selection

Bibliographic records were screened using Rayyan software. Clinical trials and funding data were screened in situ, with screening decisions recorded on an Excel spreadsheet. Due to the rapid nature of this project, one person (LT, AS, RP, or ER) screened each record.

Data extraction and quality assessment

Data were extracted and synthesised by one person (LT, RP or ER) per section (funding data, clinical trials and published evidence). Quality assessment of records was not undertaken as the scope of this project was to identify products, technologies, funding and companies as opposed to assessing the methodological quality of the evidence on this topic. The report was edited and finalised by GN.

Innovation Landscape

Clinical trials

From 2019 onwards, there were 11 clinical trials[3-13] that satisfied the inclusion criterion, covering the following artificial blood products:

- HBOC-201 (Hemopure)[14]
- Whole blood analog (unnamed)
- Marine oxygen carrier M101 (HEMO2life)[15]
- Perfluorocarbon ABL-101[16]
- PP-007 (Sanguinate)[17]
- YQ23[18]

Of the 11 trials, France and the USA hosted the most (n=3), followed by Hong Kong and the UK (n=2), then New Zealand (n=1). This seems to follow the locations where artificial blood products are developed and manufactured: HemO2life is developed by the French company Hemarina,[15] HemoPure by the USA company HbO2 Therapeutics,[14] and YQ23 by the Hong Kong company New Beta Innovation[18]. Two companies were also identified independently from the clinical trials search; NuvOx Pharma[19] (USA) who are developing a therapeutic to treat diseases relating to hypoxia, and Membio[20] (Canada) who are working on biomanufacturing blood without a donor. Most clinical trials identified had no phase listed (n=6), three were in phase 1, and one each in phase 1/2 and phase 2. No study results were published on the clinical trial sources. Study inclusion conditions (Figure 1) focused on transplant (n=3), acute ischaemic stroke (n=2), followed by advanced solid tumour, anaemia, critical limb ischaemia, haemorrhage, healthy individuals and renal disease (n=1).

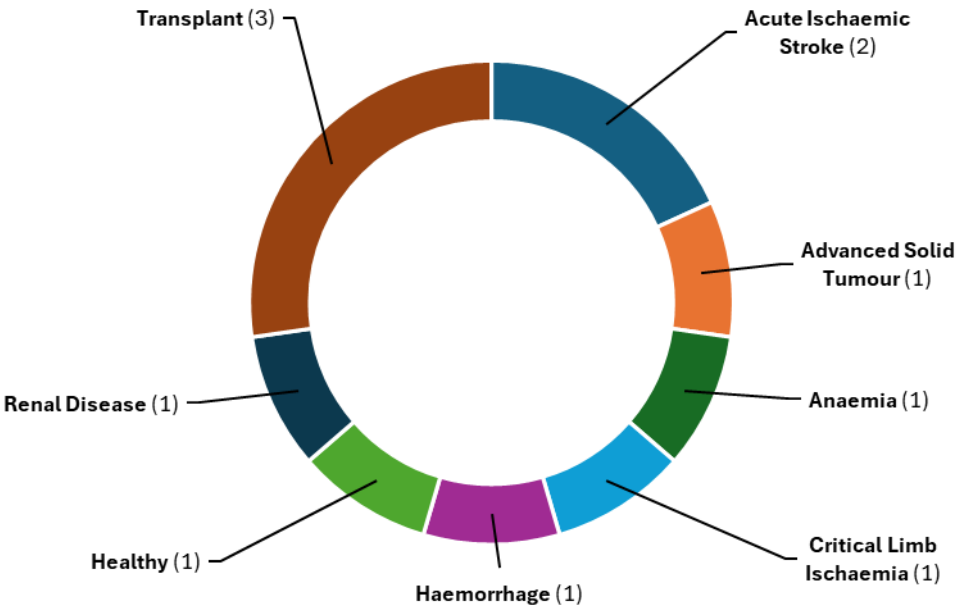

Figure 1. Conditions across the included clinical trials

Product	Condition(s)	Clinical trial ID(s)	Clinical trial status
ABL-101	Acute ischaemic stroke	NCT03463551	Unknown
HBOC-201	Anaemia	NCT01881503	Unknown
HEMO2life	Renal disease; transplant	NCT04181710; NCT05050513; NCT05469906; ACTRN12623000301662p	Completed; unknown; not yet recruiting; not yet recruiting
Whole blood analogue	Haemorrhage	NCT05756426	Recruiting
PP-007	Acute ischaemic stroke	NCT04677777	Completed
YQ23	Advanced solid tumour; critical limb ischaemia; Healthy	NCT04513067; NCT04792008; NCT03802292	Terminated; terminated; completed

Table 1: Artificial blood products by indication and stage

There were two UK-based clinical studies: one on YQ23 in healthy participants (phase 1, completed),[11] and another on ABL-101 for acute ischaemic stroke (phase 2, unknown).[12] The phase 2 clinical trial (POST-IT, NCT03463551) is sponsored by NHS Greater Glasgow and Clyde trust, collaborating with Aurum Biosciences. Its aim is to evaluate the safety and tolerability of three dose levels of ABL-101 and supplemental oxygen in acute stroke patients. By carrying substantial extra oxygen to the brain, the ABL-101 molecule may allow the visualisation of salvageable tissue and also prevent progression of stroke damage: this may have an additional direct benefit on tissue survival.[12]

A third randomised, controlled, phase 1 cross-over trial was identified, through contact with a clinical expert (in addition to those found via registry searches), called RESTORE (REcovery and survival of STem cell Originated REd cells).[21,22] Its aim is to assess the recovery and survival of

a mini-dose of RBCs, derived from CD34+ cells isolated from adult blood, against standard donated RBCs. It is hypothesised that manufactured RBCs will have a longer survival in circulation.

Funding landscape

We identified nine non-NIHR funding records for artificial blood projects, with five of these still ongoing. Whilst the highest number of funding grants was allocated by the NIH in the USA (five projects), the largest allocator of funds was the Wellcome Trust in the UK, who allocated £2,130,351 between two projects (Figure 2).[23-28] Of the nine funded projects, five were based in the USA,[25-28] three in the UK,[23,24,29] and one in Switzerland[30]. Four of the projects were led by industry sponsors with the rest being conducted by universities. All grants have been converted into GBP to allow comparisons, using May 2024 conversion rates.

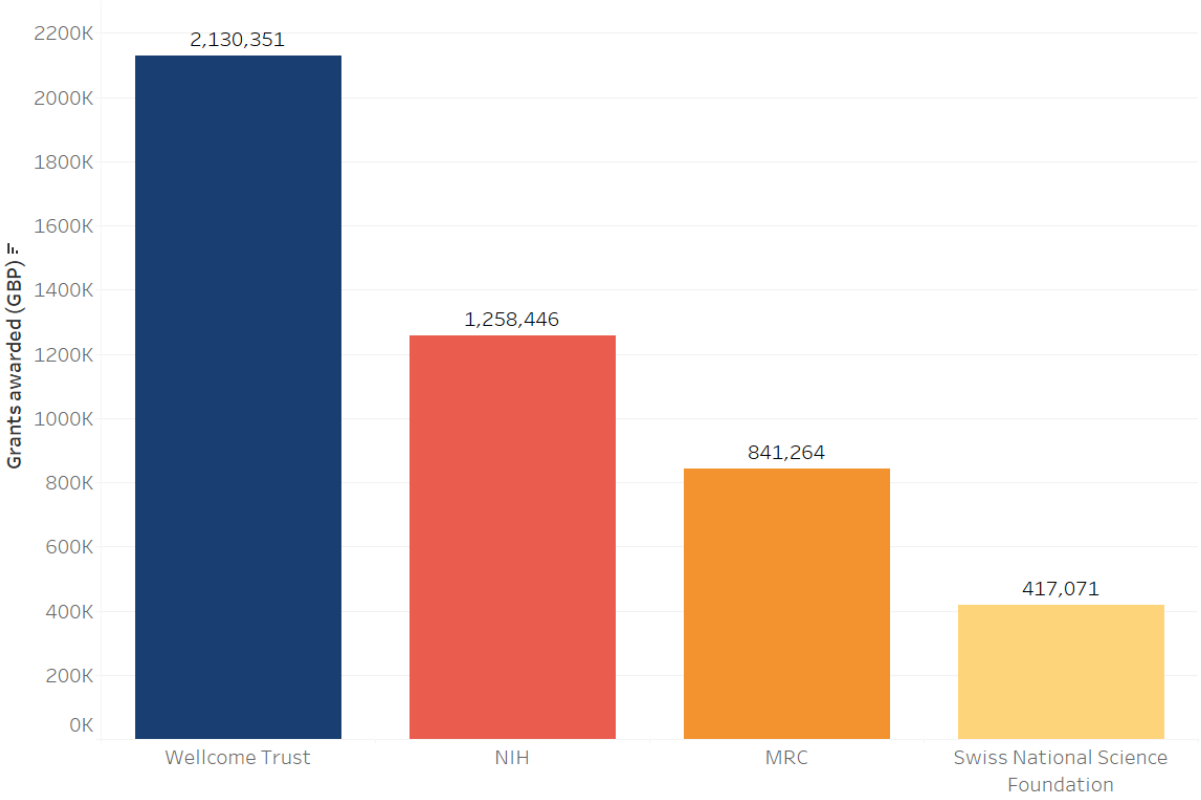

Figure 2. Graph showing the total amount of grants awarded by each funding body in GBP

The types of interventions studied included four on perfluorocarbon-based oxygen carriers, two on ErythroMer (Kalocyte, USA) or its precursor KC1003, two on GPI-ADAMTS13-Cultured Red Blood Cells and one project researching homogenous synthetic haemoglobin. Perfluorocarbon-based oxygen carriers received the highest combined level of funding, followed by Erythomer, homogenous synthetic haemoglobin and GPI-ADAMTS13-Cultured Red Blood Cells (Figure 3). The two projects for this latter technology started the earliest (2015) but no overall trend was seen in terms of type of intervention through time. There was also no

trend in funding amount with time, although most funding was awarded 2021-23 with one grant given in 2013, and two not reported.

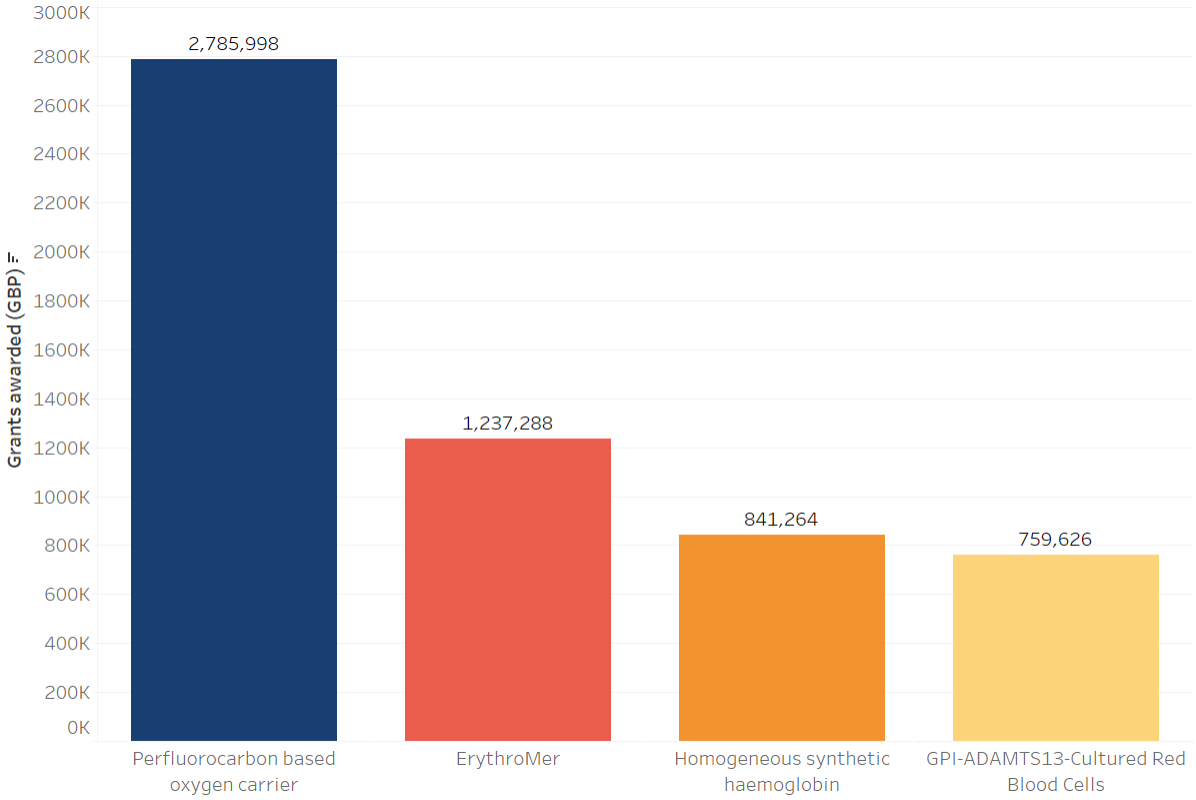

Figure 3. Level of funding awarded by technology type, shown as GBP

Published evidence

The following section identifies artificial blood products and their uses as reported in either clinical studies (in humans), *in vivo* preclinical studies or *ex-vivo* studies (involving animals or human/animal tissues). It also considers evidence from recent (published in 2023) literature reviews that implemented searches of bibliographic databases to identify studies on artificial blood products. The searches and screening were highly targeted to capture recent relevant evidence and are not comprehensive.

Literature reviews

Most research on HBOCs between 1991 and 2022 was undertaken in the USA, China, Europe, Canada and Japan.[2]

Hemopure (HBOC-201, HbO2 Therapeutics Corporation, USA) is the only commercially available HBOC that is used in human patients on a global scale;[2] Oxyglobin is approved for veterinary use in the European Union (EU) and the USA; HemO2life has recently been

approved for organ preservation in the context of transplantation in the EU; and OxyVita and Sanguinate are in clinical development. The following artificial blood products have been discontinued: HemAssist, PolyHeme, Hemolink, Hemospan, and Hemoximer.[1]

Clinical research

Clinical trials

Hemopure is an HBOC produced by polymerization of bovine Hb molecules. A retrospective analysis of clinical trial data compared mortality related to Hb deficit in patients who received Hemopure versus blood cells from human donors following orthopaedic surgery. No differences in mortality were found between groups. [31] In a separate analysis, the effectiveness of Hemopure for oxygen transportation was compared to packed red blood cells (red blood cells that have been removed from donor blood, to separate then from platelets and plasma) in human patients. The use of Hemopure was associated with a greater Hb deficit and with an increase in the number of severe adverse events compared to packed red blood cells.[32]

Hb vesicles (HbVs) are HBOCs incorporating purified and concentrated Hb solution in vesicles (fluid-filled sacs that are surrounded by a membrane). In a clinical trial, healthy male adults were injected with HbVs to assess the safety of this product and its effects on blood parameters. Adverse events observed were tolerable and spontaneously resolved and no clinically significant change was observed in any vital sign, including blood pressure.[33]

Case reports and case series

Hemopure and Sanguinate (another bovine-derived artificial oxygen carrier) have been used to treat bleeding and severe anaemia in cases where transfusion was indicated but not possible (e.g., due to religious beliefs).[34-40]

Hemopure has also been used to treat unconsciousness caused by acute severe anaemia in dying patients.[41]

A case report showed that inhaled nitric oxide allowed for the safe use of Hemopure infusion by preventing HBOC-induced pulmonary and systemic vasoconstriction. [42]

Preclinical research

In-vivo/ex-vivo studies

The viability and patient outcomes following transplantation of human livers perfused with oxygen transported by two different oxygen carriers was assessed: an artificial HBOC or RBCs (the specific HBOC used was not reported).[43]

The cardioprotective effects of perfusing hearts isolated from rats with St Thomas Solution versus polymerized Hb derived from human placental cells (PolyPHb) was compared.[44]

VS-101 is a HBOC derived from unused donated human red blood cells. The safety and ability of VS-101 to maintain circulatory function and capillary oxygen delivery in anesthetised, male Sprague Dawley rats was assessed.[45]

YQ23 is a bovine-derived HBOC formed by cross-linking tetrameric Hb. It was used to treat haemorrhagic shock in rats and pigs to assess its effects on survival, tissue and blood parameters and organ function.[46]

Discussion

A variety of artificial blood products, predominantly HBOCs, were identified that are at different stages of development. One of these (Hemopure, HBOC-201) is being used on a global scale, another (HemO2life, M101) has been approved in the EU to preserve organs for transplantation, and other products are being tested in clinical trials for the treatment of a range of conditions including cancer (YQ23) and acute ischemic stroke (Sanguinate, PP-007). Other products are being tested at the pre-clinical (animals and extracted tissues) stage. This illuminates the pipeline in artificial blood product development.

References

1 Chen L, Yang Z, Liu H. Hemoglobin-Based Oxygen Carriers: Where Are We Now in 2023? *Medicina*. 2023;59(2):396. Available from: https://doi.org/10.3390/medicina59020396.

2 Zhang Q, Ma YX, Dai Z, Zhang B, Liu SS, Li WX, et al. Tracking Research on Hemoglobin-Based Oxygen Carriers: A Scientometric Analysis and In-Depth Review. *Drug Design, Development and Therapy*. 2023;17:2549-71. Available from: https://doi.org/10.2147/DDDT.S422770.

3 Clinicaltrials.gov. *Consortium for Optimized Integration of Bio-Artificial Blood Components for Adaptive Resuscitation Therapy*. *Trial ID: NCT05756426*. 2023. Status: Recruiting. Available from: https://clinicaltrials.gov/study/NCT05756426 [Accessed 7 May 2024].

4 ANZCTR. *Marine oxygen carrier (M101) for organ preservation in liver transplantation; a randomised exploratory study*. *Trial ID: ACTRN12623000301662p*. 2023. Status: Not yet recruiting. Available from: https://www.anzctr.org.au/Trial/Registration/TrialReview.aspx?id=385454 [Accessed 7 May 2024].

5 Clinicaltrials.gov. *Evaluation at 5 and 10 Years of Renal Transplant Patients*. *Trial ID: NCT05469906*. 2022. Status: Not yet recruiting. Available from: https://clinicaltrials.gov/study/NCT05469906 [Accessed 7 May 2024].

6 Clinicaltrials.gov. *Safety Study of PP-007 in Subjects With Acute Ischemic Stroke*. *Trial ID: NCT04677777*. 2021. Status: Completed. Available from: https://clinicaltrials.gov/study/NCT04677777 [Accessed 7 May 2024].

7 Clinicaltrials.gov. *YQ23 Study in Patients With Critical Limb Ischaemia*. *Trial ID: NCT04792008*. 2021. Status: Terminated. Available from: https://clinicaltrials.gov/study/NCT04792008 [Accessed 7 May 2024].

8 Clinicaltrials.gov. *Evaluation of HEMO2Life® for Kidney Graft Preservation (OXYOP): 4 Years Follow-up*. *Trial ID: NCT05050513*. 2021. Status: Unknown status. Available from: https://clinicaltrials.gov/study/NCT05050513 [Accessed 7 May 2024].

9 Clinicaltrials.gov. *Evaluation of a Marine OXYgen Carrier for Organ Preservation*. *Trial ID: NCT04181710*. 2020. Status: Completed. Available from: https://clinicaltrials.gov/study/NCT04181710 [Accessed 7 May 2024].

10 Clinicaltrials.gov. *A Safety Study of YQ23 in Advanced Solid Tumors Patients*. *Trial ID: NCT04513067*. 2020. Status: Terminated. Available from: https://clinicaltrials.gov/study/NCT04513067 [Accessed 7 May 2024].

11 Clinicaltrials.gov. *First-In-Man, Healthy Volunteer Study to Evaluate Safety on the Use of YQ23*. *Trial ID: NCT03802292*. 2019. Status: Completed. Available from: https://clinicaltrials.gov/study/NCT03802292 [Accessed 7 May 2024].

12 Clinicaltrials.gov. *Perfluorocarbon (ABL-101) Oxygenation for Stroke: Trial With GOLD (Glasgow Oxygen Level Dependent Technology) Imaging Theranostic*. *Trial ID: NCT03463551*. 2018. Status: Unknown status. Available from: https://clinicaltrials.gov/study/NCT03463551 [Accessed 7 May 2024].

13 Clinicaltrials.gov. *Expanded Access Study of HBOC-201 (Hemopure) for the Treatment of Life-Threatening Anemia*. *Trial ID: NCT01881503*. 2013. Status: Unknown status. Available from: https://clinicaltrials.gov/study/NCT01881503 [Accessed 7 May 2024].

14 HbO2 Therapeutics. *Hemopure*. 2022. Available from: https://www.hbo2therapeutics.com/our-product [Accessed 7 May 2024].

15 Hemarina. *HEMO2life®*. 2024. Available from: https://www.hemarina.com/ours-products/hemo2life/?lang=en [Accessed 7 May 2024].

16 Aurum Biosciences. *Aurum Biosciences is developing novel therapeutics and diagnostics in areas of unmet clinical need*. 2023. Available from: https://www.aurumbiosciences.com/ [Accessed 7 May 2024].

17 Prolong Pharmaceuticals. *Pipeline*. 2024. Available from: https://prolongpharma.com/pipeline/ [Accessed 7 May 2024].

18 New Beta Innovation. *About Us*. 2024. Available from: https://www.newbetainnovation.com/ [Accessed 7 May 2024].

19 NuvOx Pharma. *A First-in-Class Oxygen Therapeutic*. 2024. Available from: https://www.nuvoxpharma.com/ [Accessed 7 May 2024].

20 University of Waterloo. *Waterloo News: Finding new ways to manufacture red blood cells*. 2021. Available from: https://uwaterloo.ca/news/global-impact/finding-new-ways-manufacture-red-blood-cells [Accessed 7 May 2024].

21 Unit NBaTCT. *RESTORE: Recovery and survival of stem cell originated red cells*. 2024. Available from: https://www.nhsbt.nhs.uk/clinical-trials-unit/current-trials-and-studies/restore/ [Accessed 7 May 2024].

22 NIHR Blood and Transplant Research Unit in Red Blood Cell Products. *RESTORE clinical trial*. 2024. Available from: https://www.bristol.ac.uk/btru/work/trial/ [Accessed 7 May 2024].

23 The Wellcome Trust. *GOLD imaging in acute stroke: further technology development incorporating a perfluorocarbon oxygen carrier (Oxycyte) [Funding. Recipient: Aurum Biosciences Limited]*. 2015. Available from: https://grantnav.threesixtygiving.org/grant/360G-Wellcome-102567_Z_13_Z [Accessed 7 May 2024].

24 The Wellcome Trust. *Development of in-vivo 19F Clinical MR imaging Using a Novel 19F/1H Coil in Combination with an Intravenous Perfluorocarbon (ABL-101) [Funding. Recipient: University of Glasgow]*. 2021. Available from: https://grantnav.threesixtygiving.org/grant/360G-Wellcome-222695_Z_21_Z [Accessed 7 May 2024].

25 NIH. *Manufacturing Scale-up, Purification, and Analytical Method Development, Validation and Qualification for KC1003, Key Precursor for ErythroMer (RBC substitute) [Funding. Recipient: KALOCYTE, INC.]*. 2017. Available from: https://reporter.nih.gov/project-details/10324723 [Accessed 7 May 2024].

26 NIH. *ErythroMer: Nanoscale BioSynthetic Red Cell Substitute [Funding. Recipient: KALOCYTE, INC.]*. 2017. Available from: https://reporter.nih.gov/project-details/10581181 [Accessed 7 May 2024].

27 NIH. *GPI-ADAMTS13-Cultured Red Blood Cells [Funding. Recipient: ALBERT EINSTEIN COLLEGE OF MEDICINE]*. 2015. Available from: https://reporter.nih.gov/project-details/10647840 [Accessed 7 May 2024].

28 NIH. *Extra-Corporeal Oxygenator with Minimal Blood Surface Contact [Funding. Recipient: BOUNDLESS SCIENCE, LLC]*. 2023. Available from: https://reporter.nih.gov/project-details/10760184 [Accessed 7 May 2024].

29 Medical Research Council. *Optimisation of the manufacture of a homogeneous synthetic haemoglobin as a novel Oxygen Therapeutic / Blood Substitute [Funding. Recipient: University of Essex]*. 2020. Available from: https://gtr.ukri.org/projects?ref=MR/T025441/1#/tabOverview [Accessed 7 May 2024].

30 Swiss National Science Foundation. *Reconditioning of marginal donor lung in ex vivo lung perfusion system using perfluorocarbon based oxygen carrier [Funding. Recipient: University of Zurich]*. 2017. Available from: https://europepmc.org/grantfinder/grantdetails?query=gid%3A%22173291%22 [Accessed 7 May 2024].

31 Jahr JS, Williams JP. Blood Component Requirements and Erythrocyte Transfusion and Mortality Related to Hemoglobin Deficit in Phase III Trial of Hemoglobin-Based Oxygen Carrier: HBOC-201. *American Journal of Therapeutics*. 2022;29(3):E279-E86. Available from: https://doi.org/10.1097/MJT.0000000000001494.

32 Dube GP, Pitman AN, MacKenzie CF. Relative efficacies of HBOC-201 and polyheme to increase oxygen transport compared to blood and crystalloids. *Shock*. 2019;52(1S):100-7. Available from: https://doi.org/10.1097/SHK.0000000000001058.

33 Azuma H, Amano T, Kamiyama N, Takehara N, Jingu M, Takagi H, et al. First-in-human phase 1 trial of hemoglobin vesicles as artificial red blood cells developed for use as a transfusion alternative. *Blood Advances*. 2022;6(21):5711-5. Available from: https://doi.org/10.1182/bloodadvances.2022007977.

34 Bachert SE, Dogra P, Boral LI. Alternatives to Transfusion. *American Journal of Clinical Pathology*. 2020;153(3):287-93. Available from: https://doi.org/10.1093/ajcp/aqz175.

35 Barrett CD, Theodore S, Dechert T, Burke P, Khoury R, Cap AP, Scantling D. Resuscitation of an exsanguinated obstetrics patient with HBOC-201: A case report. *Transfusion*. 2022;62(S1):S218-S23. Available from: https://doi.org/10.1111/trf.16973.

36 Kaufman M, Smith JA, Walker A, Barkai L, Beri S, Bronshteyn I, et al. Single Center 8 Year Experience with HBOC-201 for Patients for Whom Blood Transfusion is Not an Option. *Anesthesia and Analgesia*. 2022;135(3 Supplement 1):80-1. Available from: https://doi.org/10.1213/01.ane.0000872644.39327.c9.

37 McConachie S, Wahby K, Almadrahi Z, Wilhelm S. Early Experiences With PEGylated Carboxyhemoglobin Bovine in Anemic Jehovah's Witnesses: A Case Series and Review of the Literature. *Journal of Pharmacy Practice*. 2020;33(3):372-7. Available from: https://doi.org/10.1177/0897190018815373.

38 Sticco K, Gokhale A, Ahmed T, Spitzer E. The management of acute blood loss with hemoglobin-based oxygen carriers in Jehovah's witness patients: A case series and review of literature. *American Journal of Clinical Pathology*. 2019;152(Supplement 1):S18. Available from: https://doi.org/10.1093/ajcp/aqz112.034.

39 Sun J, Cho B, Cruz N, Resar L, Frank S. Hemoglobin Based Oxygen Carrier Treatment and Clinical Outcomes in Severe Anemia When Blood is Not an Option. *Anesthesia and Analgesia*. 2022;135(3 Supplement 1):9-10. Available from: https://doi.org/10.1213/01.ane.0000872644.39327.c9.

40 Zumberg M, Gorlin J, Griffiths EA, Schwartz G, Fletcher BS, Walsh K, et al. A case study of 10 patients administered HBOC-201 in high doses over a prolonged period: outcomes during severe anemia when transfusion is not an option. *Transfusion*. 2020;60(5):932-9. Available from: https://doi.org/10.1111/trf.15778.

41 Weiskopf RB, Davenport R, Cap AP, Reddy V, Waters JH, Cserti-Gazdewich C. Increasing hemoglobin concentration with an artificial oxygen carrier improves severe anemia-induced degraded cognitive function. *Journal of Trauma and Acute Care Surgery*. 2021;91(2 Supplement 2):S182-S5. Available from: https://doi.org/10.1097/TA.0000000000003261.

42 Marrazzo F, Larson G, Sherpa Lama TT, Teggia Droghi M, Joyce M, Ichinose F, et al. Inhaled nitric oxide prevents systemic and pulmonary vasoconstriction due to hemoglobin-based oxygen carrier infusion: A case report. *Journal of Critical Care*. 2019;51:213-6. Available from: https://doi.org/10.1016/j.jcrc.2018.04.008.

43 van Leeuwen OB, Bodewes S, Haring MP, Bruggenwirth IM, Lantinga VA, Thorne AM, et al. A Clinical Comparison of Two Different Oxygen Carriers for Combined Hypothermic and Normothermic Machine Perfusion of High-risk Donor Livers. *HPB*. 2021;23(Supplement 3):S689. Available from: https://doi.org/10.1016/j.hpb.2021.08.038.

44 Wang Y, Zhao X, Li F, Chen W, Wang L, Yang C. Polymerized Human Placenta Hemoglobin (PolyPHb) Attenuates Myocardial Infarction Injury in Rats. *Artificial Cells, Blood Substitutes, and Biotechnology*. 2012;40(1-2):7-13. Available from: https://doi.org/10.3109/10731199.2011.579567.

45 Nugent WH, Sheppard FR, Vandegriff KD, Schindler WM, Malavalli A, Song BK. Exchange transfusion with VS-101: A new pegylated-hb designed to restore perfusion and increase O_2 carrying capacity. *Shock*. 2024;61(2):304-10. Available from: https://doi.org/10.1097/SHK.0000000000002293.

46 Li T, Yang G, Zhu Y, Tzang FC, Lau S-H, Kwok S-Y, et al. Beneficial effects of novel cross-linked hemoglobin YQ23 on hemorrhagic shock in rats and pigs. *Journal of Surgical Research*. 2017;210:213-22. Available from: https://doi.org/10.1016/j.jss.2016.11.045.

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This work was undertaken using a rapid approach. Although undertaken using a systematic approach, processes within the cycle of conducting a horizon scan have all been abbreviated, limiting our certainty about the evidence presented; ultra rapid evidence synthesis approaches have been used to consider the published literature. There has been no formal quality assessment of the information included within this innovation briefing and no quality assurance processes have been undertaken as part of the methodological approach.

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