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Editorial

Sickle cell disease (SCD), is an inherited hemoglobinopathy which occurs when a person inherits two abnormal copies of the β-globin gene (*HBB*) that makes haemoglobin, one from each parent. About 80% of SCD cases are believed to occur in Sub-Saharan Africa. It also occurs to a lesser degree in parts of India, Southern Europe, West Asia, and North Africa. Until now there were no curative treatments available for SCD. Recently, the FDA has approved the first gene therapies (*Casgevy and Lyfgenia*) for the treatment of SCD, in patients 12 years and older. All current gene therapy and gene editing approaches for SCD require autologous hematopoietic cell transplantation with myeloablative conditioning.

Hepatocellular carcinoma (HCC) is the most common type of primary liver cancer in adults and is the most common cause of death in people with cirrhosis. It is also the third leading cause of cancer-related deaths worldwide. The treatment and prognosis of HCC vary depending on the specifics of tumour histology, size, the extent of its involvement and spread, and overall health of the patient. The vast majority of HCC cases and the lowest survival rates after treatment occur in Asia and sub-Saharan Africa, in countries where Hepatitis B infection is endemic and many are infected from birth. The incidence of HCC in the United States and other developing countries is increasing due to an increase in Hepatitis C virus infections. In a randomized, double-blind, phase 3 trial *Lenvatinib plus Pembrolizumab vs. Lenvatinib* plus Placebo was done for advanced HCC. *Pembrolizumab to Lenvatinib* as first-line therapy for advanced HCC was found to show promising clinical activity; *Lenvatinib plus Pembrolizumab* did not meet prespecified significance for improved overall survival and progression-free survival versus *Lenvatinib plus placebo*. Unlike Hepatitis B and C, Hepatitis A infection is a self-limiting disease, however, presence of co-infection, underlying liver disease and consumption of certain drugs can cause severe complications. Hence, all cases should be followed up till complete recovery, as suggested from a study on 'Clinical Spectrum of the Disease in Children Admitted in a Tertiary Care Hospital'.

NICE has published newer guidelines for several diseases like 'Bipolar disorder: assessment and management', 'Middle meningeal artery embolization for chronic subdural haematomas', and 'Primary spontaneous pneumothorax'.

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I. Drugs

FDA Approves First Gene Therapies to Treat Patients with Sickle Cell Disease
Source: The FDA, December 2023
Link: https://www.fda.gov/news-events/press-announcements/fda-approves-first-gene-therapies-treat-patients-sickle-cell-disease

Casgevy and Lyfgenia, representing the first cell-based gene therapies for the treatment of sickle cell disease (SCD) in patients 12 years and older. Casgevy, is the first FDA-approved treatment to utilize a type of novel genome editing technology, signaling an innovative advancement in the field of gene therapy. Casgevy, a cell-based gene therapy, is approved for the treatment of sickle cell disease in patients 12 years of age and older with recurrent vaso-occlusive crises. Casgevy is the first FDA-approved therapy utilizing CRISPR/Cas9, a type of genome editing technology. Patients' hematopoietic (blood) stem cells are modified by genome editing using CRISPR/Cas9 technology.

Empagliflozin for treating chronic kidney disease
Source: The NICE, December 2023
Link: https://www.nice.org.uk/guidance/ta942

Empagliflozin (Jardiance, Boehringer Ingelheim) is indicated for the treatment of 'chronic kidney disease (CKD) in adults'.

II. Clinical Research

Addition of danicopan to ravulizumab or eculizumab in patients with paroxysmal nocturnal haemoglobinuria and clinically significant extravascular haemolysis (ALPHA): a double-blind, randomised, phase 3 trial
Source: The Lancet, December 2023
Link: https://www.thelancet.com/journals/lanhae/article/PIIS2352-3026(23)00315-0/fulltext

These primary efficacy and safety results show that danicopan as add-on treatment to ravulizumab or eculizumab significantly improved haemoglobin concentrations at week 12 with no new safety concerns, suggesting an improved benefit–risk profile in patients with PNH and clinically significant extravascular haemolysis.

Lenvatinib plus pembrolizumab versus lenvatinib plus placebo for advanced hepatocellular carcinoma (LEAP-002): a randomised, double-blind, phase 3 trial
Source: The Lancet, December 2023
Link: https://www.thelancet.com/journals/lanonc/article/PIIS1470-2045(23)00469-2/fulltext

Pembrolizumab to lenvatinib as first-line therapy for advanced hepatocellular carcinoma has shown promising clinical activity; lenvatinib plus pembrolizumab did not meet prespecified significance for improved overall survival and progression-free survival versus lenvatinib plus placebo.

Efficacy and safety of baricitinib or ravulizumab in adult patients with severe COVID-19 (TACTIC-R): a randomised, parallel-arm, open-label, phase 4 trial
Source: The Lancet, December 2023
Link: https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(23)00376-4/fulltext

Neither baricitinib nor ravulizumab, as administered in this study, was effective in reducing disease severity in patients selected for severe COVID-19. Safety was similar between treatments and standard of care. The short period of dosing with baricitinib might explain the discrepancy between our findings and those of other trials.

The therapeutic potential of targeting complement C5 activation product C5a, rather than the cleavage of C5, warrants further evaluation.

Rare secondary T cell lymphomas after chimeric antigen receptor (CAR)-T cell therapy
Source: The Uptodate, December 2023
Link: https://www.uptodate.com/contents/whats-new-in-drug-therapy
https://www.uptodate.com/contents/diffuse-large-b-cell-lymphoma-dlbcl-suspected-first-relapse-or-refractory-disease-in-patients-who-are-medically-fit?sectionName=RELAPSE%20%3C12%20MONTHS%20OR%20PRIMARY%20REFRACTORY%20DLBCL&topicRef=8360&anchor=H3334776372&source=see_link#H3334776372

Chimeric antigen receptor (CAR)-T cell therapy is effective for treatment of relapsed or refractory B cell lymphomas, multiple myeloma, and other disorders, but it may be associated with severe and potentially fatal adverse effects (AEs). Reports are now emerging of secondary T cell lymphomas in patients treated with CD19- and B cell maturation antigen (BCMA)-directed CAR-T cell therapy, some of which have CAR-positive malignant cells. US Food and Drug Administration (FDA)-approved CAR-T cell products include warnings about potential secondary malignancies, but at present, no regulatory action has been taken and no product has been recalled. Patients receiving CAR-T cell therapy should be monitored for development of new malignancies, and any such events should be reported to the manufacturer and to the FDA AE Reporting System (FAERS)

Gene therapy and gene editing in sickle cell disease
Source: The Uptodate, December 2023
Link: https://www.uptodate.com/contents/whats-new-in-hematology
https://www.uptodate.com/contents/investigational-therapies-for-sickle-cell-disease?sectionName=Gene%20therapy%20and%20gene%20editing&topicRef=8359&anchor=H1521590660&source=see_link#H1521590660

Lovotibeglogene autotemcel (lovo-cel) uses lentivirus-based gene therapy to introduce the antisickling beta globin variant T87Q and produce hemoglobin A with antisickling properties. Exagamglogene autotemcel (exa-cel) uses gene editing to disrupt the BCL11A gene and reverse the gamma globin to beta globin switch. All current gene therapy and gene editing approaches for SCD require autologous hematopoietic cell transplantation with myeloablative conditioning.

Hepatitis A: A Clinical Spectrum Of The Disease In Children Admitted In A Tertiary Care Hospital
Source: The New Indian Journal of Pediatrics, December 2023
Link: https://nijp.org/hepatitis-a-a-clinical-spectrum-of-the-disease-in-children-admitted-in-a-tertiary-care-hospital/

Though hepatitis A infection is a self-limiting disease, presence of co-infection, underlying liver disease and consumption of certain drugs can cause severe complications. Hence, all cases should be followed up till complete recovery.

Additional Bicarbonate Infusion Complements WHO Rehydration Therapy in Children with Acute Diarrhea and Severe Dehydration Presenting with Severe Non-anion Gap Metabolic Acidemia: An Open Label Randomized Trial
Source: Indian Journal of Pediatrics, December 2023
Link: https://link.springer.com/article/10.1007/s12098-023-04925-x

Additional calculated dose of bicarbonate infusion led to significantly early resolution of metabolic acidemia, lesser utilization of critical care facilities, and lesser adverse outcome in children with ADSD and sNAGMA, compared to standard therapy, with no adverse effect.

Procalcitonin Guided Antibiotic Stewardship in Pediatric Sepsis and Lower Respiratory Tract Infections
Source: Indian Journal of Pediatrics, December 2023
Link: https://link.springer.com/article/10.1007/s12098-023-04960-8

PCT-ASP reduces the duration of antibiotics and duration of hospital stay without increasing morbidity and mortality.

III. Devices

Digitally enabled therapies for adults with depression: early value assessment
Source: The NICE, December 2023
Link: https://www.nice.org.uk/guidance/hte8

Digitally enabled therapies are a treatment option for adults with depression. They are technologies, used online or through apps, that deliver a substantial portion of therapy through their content. They are delivered with support from a trained practitioner or therapist in NHS Talking Therapies for anxiety and depression services (formerly Improving Access to Psychological Therapies, or IAPT). The practitioner or therapist facilitates the intervention, encourages completion, recommends complementary material, and reviews progress and outcomes.

IV. Treatment Guidelines

Bipolar disorder: assessment and management
Source: The NICE, December 2023
Link: https://www.nice.org.uk/guidance/cg185

This guideline covers recognising, assessing and treating bipolar disorder (formerly known as manic depression) in children, young people and adults. The recommendations apply to bipolar I, bipolar II, mixed affective and rapid cycling disorders. It aims to improve access to treatment and quality of life in people with bipolar disorder.

Middle meningeal artery embolisation for chronic subdural haematomas
Source: The NICE, December 2023
Link: https://www.nice.org.uk/guidance/ipg779

Middle meningeal artery embolisation for chronic subdural haematomas. This involves injecting particles into the middle meningeal artery to block it

Guidelines for primary spontaneous pneumothorax
Source: The Uptodate, December 2023
Link: https://www.uptodate.com/contents/whats-new-in-pulmonary-and-critical-care-medicine
https://www.uptodate.com/contents/treatment-of-primary-spontaneous-pneumothorax-in-adults?sectionName=INITIAL%20EVALUATION%20AND%20MANAGEMENT&topicRef=8355&anchor=H891236955&source=see_link#H891236955

The British Thoracic Society (BTS) has recently issued new guidelines for the management of primary spontaneous pneumothorax (PSP). Major changes since 2010 include a symptom- rather than size-based approach. For patients with mild symptoms who are stable following adequate analgesia, monitored observation is preferred, while those with significant dyspnea should undergo a drainage procedure.

V. Healthcare Administration

Does Suicide Risk Screening Improve the Identification of Primary Care Patients Who Will Attempt Suicide Versus Depression Screening Alone?
Source: The JCI, December 2023
Link: https://www.jointcommissionjournal.com/article/S1553-7250(23)00206-4/fulltext

Depression screening with the PHQ-9 was the most effective strategy for identifying patients who attempted suicide in the near term. Universal suicide risk screening is unlikely to meaningfully improve identification of higher-risk patients beyond PHQ-9 depression screening.