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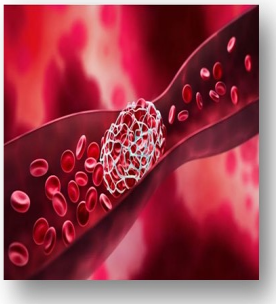
Switching from alteplase to tenecteplase as the standard thrombolytic therapy for acute ischemic stroke



Acute ischemic stroke (AIS) poses a significant public health challenge, adversely impacting the national economy and public welfare due to its high incidence, disability, mortality rates, and escalating medical expenses. Intravenous thrombolysis represents a safe and effective approach for AIS's ultra-early treatment.

Following the US FDA approval of the recombinant tissue plasminogen activator (alteplase, rt-PA), extensive researches have confirmed that alteplase can significantly improve clinical outcomes. However, its specificity for fibrin is moderate and the risk of intracranial hemorrhage still exists. Alteplase has a short half-life (4-5 min), and its administration is complex, requiring intravenous bolus followed by a continuous infusion for one hour; the efficiency of this ultra-early treatment workflow still needs improvement.

Tenecteplase, a DNA variant of alteplase, exhibits a higher fibrin specificity and greater resistance to plasminogen activator inhibitor-1 (PAI-1), effectively targeting thrombi. Its improved fibrin specificity minimizes systemic fibrinogen consumption, substantially reducing hemorrhage risk. Additionally, tenecteplase's extended plasma half-life permits a 5-10 second intravenous injection administration providing the convenience of single bolus administration that may allow patients to get the blood clot or thrombus removed earlier with shorter times for vessel opening that could reduce potential risks.

As a third-generation anti-fibrinolytic intravenous thrombolytic drug, tenecteplase boasts a well-characterized mechanism of action and significant practical advantages in administration, making it a promising candidate.

Multiple studies have confirmed that its efficacy and safety may not be inferior to that of alteplase. And it has potential workflow advantages. The bolus thrombolytic agent tenecteplase narrowly failed to show noninferiority to alteplase in the tenecteplase versus alteplase for stroke thrombolysis evaluation (TASTE) clinical trial within 4.5 hours of symptom onset selected by perfusion imaging in patients with acute ischemic stroke.

The TASTE was a multicenter, randomized, controlled phase 3 noninferiority trial that used advanced perfusion imaging to select stroke patients, which gives a precise identification of ischemic stroke and excludes patients who may have conditions that mimic stroke conducted in 35 hospitals in eight countries. Patients were randomized to receive intravenous tenecteplase (0.25 mg/kg) or alteplase (0.90 mg/kg). However, the trial was stopped early after previous studies had shown the noninferiority of tenecteplase to alteplase, thus reducing its power. In addition, the per-protocol analysis did meet noninferiority criteria after 680 of the planned 830 patients had been enrolled following the results of previous tenecteplase trials. In the intention-to-treat analysis, the primary outcome occurred in a numerically higher proportion of patients allocated to tenecteplase (57.0%) than those allocated to alteplase (55.3%). Also, an updated meta-analysis of all the studies comparing the two thrombolytics, including these latest TASTE results, has demonstrated for the first time that tenecteplase is superior to alteplase for excellent recovery 3 months after stroke.

The TASTE trial and the updated meta-analysis were presented on May 15 at the European Stroke Organization Conference (ESOC) 2024 annual meeting.

Faster Time to Treatment

The updated meta-analysis of all the tenecteplase vs alteplase studies showed a full recovery that was achieved in 59% of tenecteplase patients vs 55% of alteplase patients. Tenecteplase is administered via a single bolus injection, it is easier and quicker to administer than alteplase, which is given as a bolus plus an infusion, thus saving 7 minutes compared to giving alteplase in the urgent treatment of patients with acute stroke. These new results and the updated meta-analysis give us new evidence that will accelerate the transition to tenecteplase when the worldwide shortage resolves.

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Ph. Mai Mousa, PharmD., M.Sc, PhD. Cand.

GLP-1 agonists and fertility

A growing number of women are reportingunplanned pregnancies even among those who've struggled with fertility while taking using glucagon-like peptide 1 (GLP-1) receptor agonist drugs like wegovy and ozempic. The new trend has been dubbed “Ozempic babies” on social media.

GLP-1 agonists are a class of medications utilized to treat type 2 diabetes mellitus (T2DM) and obesity, bind to and activate the GLP-1 receptor, enhancing insulin secretion and slowing gastric emptying. GLP-1s may make birth control pills less effective. A suggested explanation states that as these medications slow down stomach emptying, so they affect how food and medications are absorbed, this causes oral birth control pills to not be absorbed consistently, especially each time the dose of GLP-1 agonists are stepped up, this is resulting in failure of oral birth control pills.

Furthermore, it is well-established that weight plays a significant role in fertility, excess weight can lead to insulin resistance; for women, insulin resistance is often accompanied by imbalances in reproductive hormones, contributing to difficulties in conceiving. As GLP-1 agonists contribute to weight loss by reducing appetite and calorie intake, which can lead to improved insulin sensitivity. For many, this improvement may also rebalance hormonal levels, creating a more favorable environment for conception, and many women who are anovulatory start to have regular ovulation and menses, which takes them from a low fertility situation to a more normal fertile state. Some doctors have begun prescribing the drugs off-label for women with polycystic ovary syndrome (PCOS), a hormonal disorder that is a leading cause of infertility.

The prescribing label for Eli Lilly's anti-obesity drug zepbound carries a warning that patients taking birth control pills should use a backup method like condoms and that pregnant patients should stop taking the drug. Novo Nordisk, the maker of wegovy and ozempic said it has limited data because patients who were pregnant or intended to become pregnant were excluded from clinical trials.

However, animal studies done with wegovy suggest that there may be risks to using it. A study looking into the safety of wegovy during human pregnancy is ongoing and not due to be completed until August 2027.

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Ph. Amr Noweir, B.Sc.

AstraZeneca vaccine... A story comes to the end !

The AstraZeneca COVID-19 vaccine, also known as Vaxzevria, has been a critical tool in the global fight against the COVID-19 pandemic. However, its association with rare thrombotic events, particularly thrombosis with thrombocytopenia syndrome (TTS), has raised significant concerns and prompted extensive research.

Incidence and Clinical Manifestations:

Several studies have reported unusual thrombotic events associated with thrombocytopenia following vaccination with Vaxzevria. These events include cerebral venous sinus thrombosis (CVST) and splanchnic vein thrombosis, often accompanied by severe clinical outcomes such as serious bleeding and disseminated intravascular coagulation (DIC). The European Medicines Agency (EMA) has acknowledged a possible link between the vaccine and these rare thrombotic events, categorizing them as very rare side effects.

Case reports have documented the clinical manifestations and management of TTS following Vaxzevria vaccination. For instance, a study described three women who developed intracranial venous sinus thrombosis after their first dose of the vaccine. These patients exhibited elevated levels of D-dimers, Platelet-activating antibodies against platelet factor4 (PF4) antiplatelet antibodies, and thrombocytopenia. They were treated with heparinization and endovascular recanalization, leading to normalization of platelet counts. Another case report highlighted a patient who developed vaccine-induced immune thrombotic thrombocytopenia (VITT) with acute cerebral venous thrombosis and hemorrhage after receiving two doses of Vaxzevria followed by a Moderna booster. This patient required plasmapheresis, pulse steroid therapy, and intravenous immunoglobulin for management.

Interestingly, the occurrence of these thrombotic events appears to be more frequent in females than in males. Studies have shown that the incidence of potential thrombotic events in females is approximately double that in males. This gender disparity may be influenced by genetic factors, such as tissue-factor gene polymorphisms, which are more common in women.

Pathophysiological Mechanisms

The pathogenesis of TTS following Vaxzevria vaccination is thought to involve the development of PF4, a condition that clinically mimics autoimmune heparin-induced thrombocytopenia (HIT). This phenomenon is referred to as VITT. Additionally, the adenoviral vector used in the vaccine may contribute to the pro-coagulant activity by inducing tissue factor (TF) expression in endothelial cells.

Latest Updates in 2024

In 2024, AstraZeneca has initiated a global withdrawal of its COVID-19 vaccine, Vaxzevria, due to, according to the company, a decline in demand and the availability of newer vaccines targeting emerging variants of the virus. But it is believed that this decision was also driven by the harm of vaccine's reputation by reports of rare but serious side effects, particularly TTS. This rare side effect led to several countries suspending its use and eventually contributed to its global withdrawal.

Legal actions have been initiated by individuals who developed clots following vaccination, alleging that AstraZeneca failed to adequately inform them of the potential risks. The company has acknowledged the link between the vaccine and TTS in court documents but maintains that the benefits of the vaccine outweigh the risks.

The European Medicines Agency (EMA) and other health authorities have declared the vaccine no longer authorized for use within the EU. The UK and other countries have also ceased its use, favoring mRNA vaccines like Pfizer and Moderna for their higher efficacy and updated formulations.

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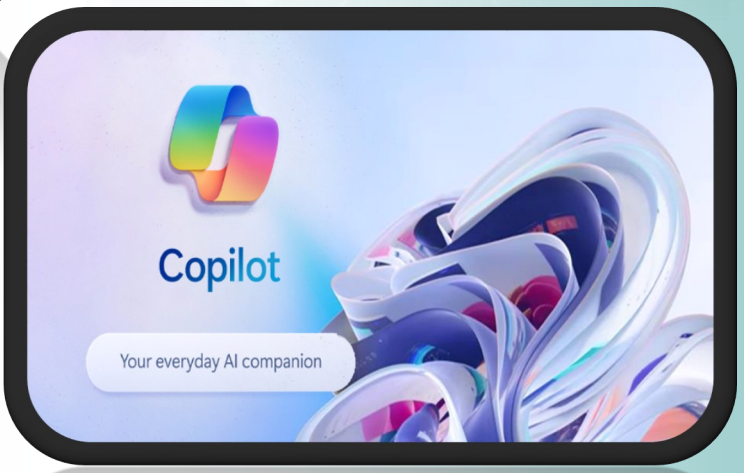
Important artificial intelligence (AI) tools for academic research



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Vision

The vision of Tanta University DPIC is to improve national healthcare service through provision of evidence-based, unbiased, patient oriented drug information services & adverse drug reporting system.

Mission

* Responding to drug inquiries related to the use of the drug and providing the health care professionals and patients with drug information related to the patient's care to achieve the optimal use of the drug in addition to the provision of other toxicological managing information.
* Educational activities to support the rational optimal use of drugs as well, supporting research activities.
* Continuous medical education and training courses in various fields of pharmacy for students, undergraduates, postgraduate students, and researchers.
* Issuing a Drug Information Bulletin periodically to take a look at medical & pharmaceutical news.
* Supporting the National Pharmaceutical Vigilance Program by following up and monitoring side effects and problems related to use of pharmaceutical preparations within regional hospitals.
* Contributing to the establishment of various treatment protocols and prescription booklet services in regional hospitals.

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