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Perspective

Overview on Molecular Targeted Therapies

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INTRODUCTION

In a variety of cancers, molecular targeted therapy improved overall and disease free survival. Molecular targeted therapy may be associated with adverse effects requiring ICU admission, although being typically well tolerated when compared to chemotherapy. Educating doctors about the clinical characteristics of these hazardous episodes may help to retain awareness and promote early detection, diagnosis, and treatment.

With the development of molecular targeted medicines, the survival of patients with solid tumours has improved dramatically over the previous decade. These targeted medicines have a lower toxicity profile than traditional cytotoxic chemotherapy, which means they can deliver higher dose intensity while also improving quality of life. An ever increasing number of patients will receive single or combined molecular treatments as a result of the rise of effective cancer screening around the world, the ageing population, the improvement in overall survival of patients with solid tumours, and a better understanding of molecular and cellular pathways involved in tumours progression. These new therapeutic medications increase progression free survival in a variety of cancers, but they also cause Adverse Effects (AEs) that range in kind and severity.

DESCRIPTION

The majority of these AEs are of low to moderate severity, graded as grade 1 to 2 toxicities by the National Cancer Institute's Common Terminology Criteria of Adverse Events. They affect numerous organ systems, including the skin, gastrointestinal tract, peripheral nervous system, liver, and endocrine system, and have been widely described in the literature, including in crucial phase II and III clinical trials. These AEs are usually predictable and expected, as they correspond to so-called on-target toxicity, which occurs when a biological mechanism is inhibited. Although the majority of adverse events are well managed in an outpatient setting, some AEs can cause severe morbidity or even death. Clinical studies, which only include carefully selected patients with mid-term clinical follow-up, seldom report life-threatening drug-related toxicities. As a result, there are little data on major drug-related adverse events in real-life patients who would not have been eligible for clinical trials. The recent development of immune checkpoint inhibitors in various settings and for various types of cancer has resulted in the emergence of a new spectrum of immunotherapy related Adverse Events (irAEs) as a result of self-tolerance impairment due to reduced cytotoxic T cell inhibition; however, given the novelty of this class, the risk of life-threatening or fatal autoimmune like AEs is unknown at this time. As a result, information on the kind, clinical presentation, management, and consequences of potentially life-threatening Adverse Events (AEs) associated with molecular targeted medicines, particularly those needing several injection, is required. In the coming years, intensivists will be responsible for a growing number of patients who are receiving innovative single or combined targeted medicines. As a result, practitioners should be aware of the potential side effects of these new medications in order to provide quick diagnosis and treatment. Additionally, discovering reliable predictive indicators of efficacy and toxicity is critical for improving patient selection and assisting oncologists in treatment decision-making.

The goal of this systematic review was to find published examples of life-threatening AEs leading to ICU hospitalization in patients with solid tumours who had received targeted anticancer therapy. Up until March 2019, all case reports and case series of drug-related Adverse Events (AEs) resulting in ICU admission in patients with solid cancer after treatment with an FDA approved molecular targeted therapy were included, with no language constraints. The study included patients admitted to a High Dependency Unit (HDU) or a Coronary Care Unit (CCU). We excluded pediatric instances, situations involving pregnancy, and those involving non-oncological molecular therapy indications. All of the above mentioned targeted therapies were given to the patient in a clinical study, off label, or as routine care, regardless of whether they were given in a clinical study, off label, or as usual care.

CONCLUSION

Case reports involving non FDA approved combinations of targeted medicines or hormonal treatments were omitted. We

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also gathered grade III–IV side effects described in the randomized controlled trial for each type of targeted therapy. We gathered clinical data on the patients who had been reported (age, gender, cancer localization, prior or concomitant anticancer treatments by chemotherapy, radiotherapy or corticosteroids). Drug-related AEs were characterized by molecular therapy family (clinical presentation at ICU admission, time since treatment initiation, and diagnosis of complication), ICU toxicity management (required organ support, surgery, anti-infectious or immunosuppressive treatment, corticosteroids use), and outcomes.