Bruton Tyrosine Kinase Inhibitors: Key Points

Clinical Considerations

- The development of BTK inhibitors has led to dramatic improvements in the management of B-cell malignancies
- Available evidence suggests that second-generation agents may have improved tolerability over the first-in-class agent ibrutinib
- Emerging evidence suggests that third-generation BTK inhibitors (currently in clinical development) may have a role in countering acquired resistance

Plain Language Summary

Background and rationale

- Bruton tyrosine kinase (BTK) is a key signalling molecule in the B-cell receptor pathway which is important for B-cell proliferation and survival.
- The development of drugs which inhibit BTK has led to dramatic improvements in the management of B-cell malignancies, difficult-to-treat diseases that primarily affect older populations.
- Following ibrutinib (the first-in-class BTK inhibitor), second-generation agents (including acalabrutinib, zanubrutinib, tirabrutinib and orelabrutinib) have been developed, primarily with an aim to improve drug tolerability.
- More recently, third-generation agents (including pirtobrutinib and nemtabrutinib) have entered later-stage clinical development, aiming to provide further treatment options.

Clinical findings

- BTK inhibitors have shown strong activity in a range of B-cell malignancies.
- The agents have acceptable tolerability, with adverse events generally being manageable with dosage modification.

Outline

This review article summarises the evidence supporting the role of BTK inhibitors (those marketed, or in later-stage clinical development) in the management of B-cell malignancies, a rapidly developing field.