# The Safety of Immunosuppressants Use in the Treatment of Immune-Related Adverse Events due to Immune Checkpoin Inhibitors: A Systematic Analysis

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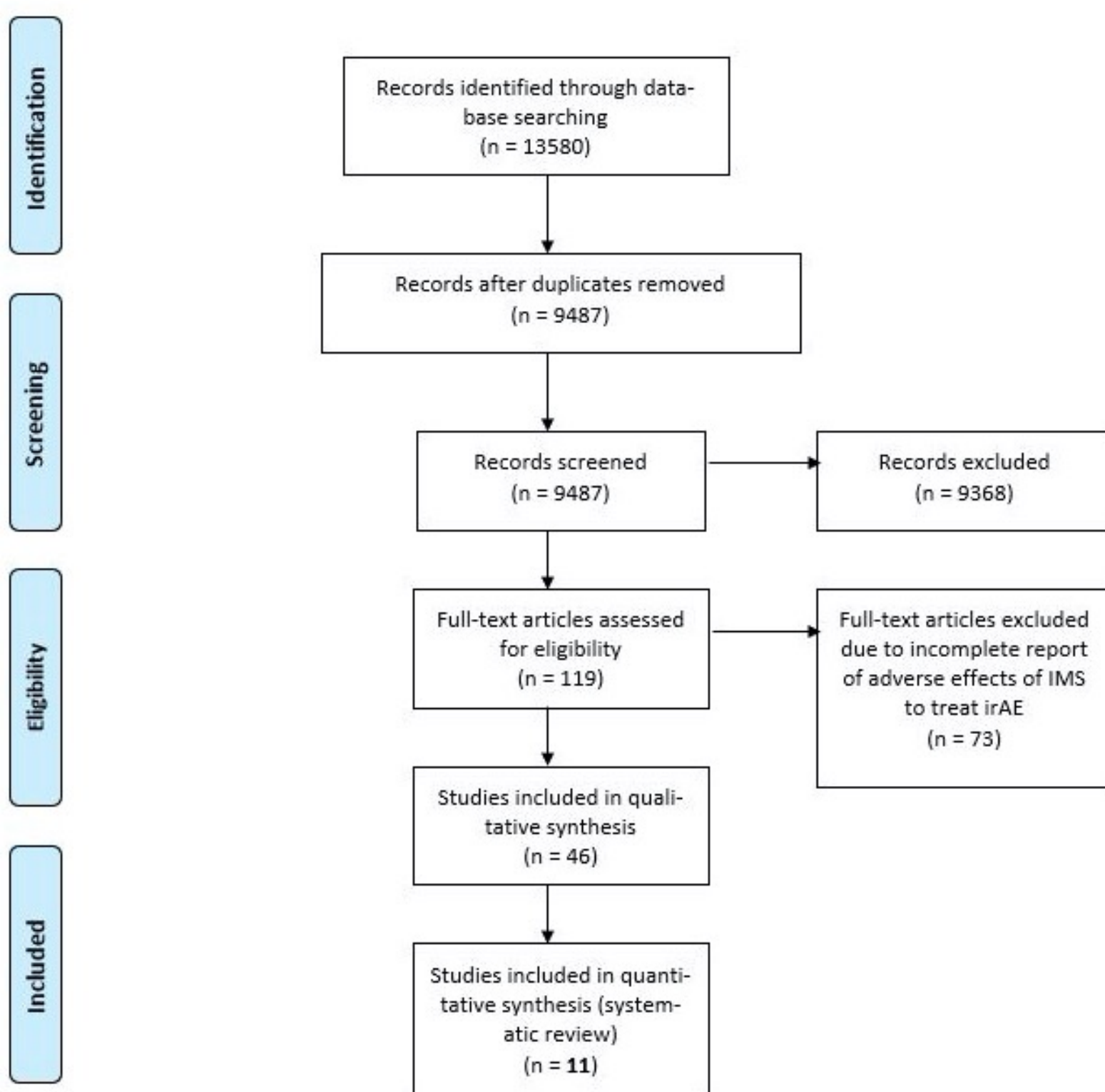
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## Introduction

- Incidence of immune related adverse events (irAE) due to immune checkpoint inhibitors (ICI) is near 30% with severe ones in 7% of patients.
- Treatment involves aggressive immunosuppression which ultimately convey in different side effects on already ill patients.
- The safety of common agents used for treatment of irAE is unknown. We aim to describe the outcomes of patients with irAE treated with immunosuppressive therapy.
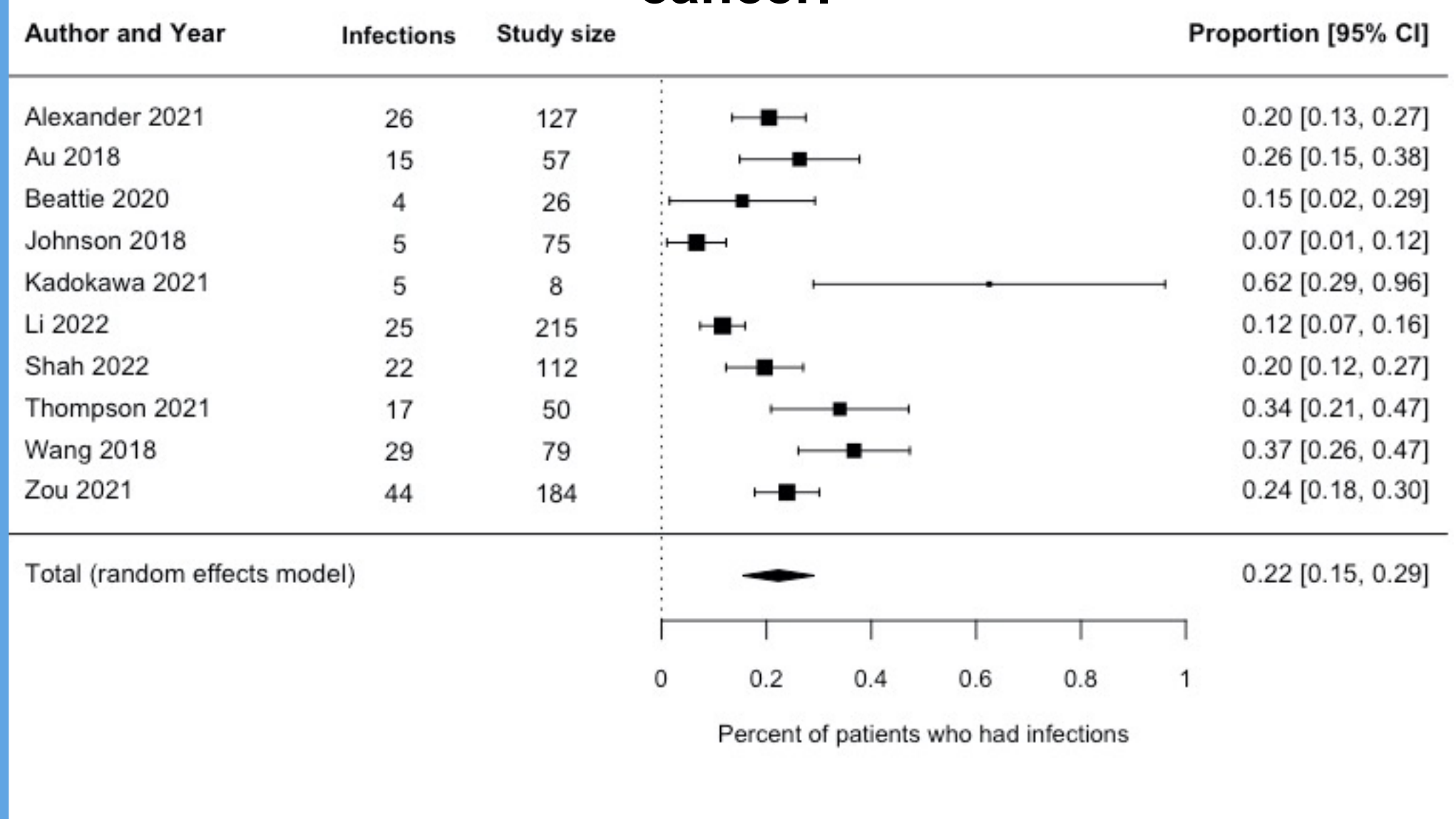
## Methods

- A systematic review was performed of studies reporting irAEs and their medical management with immunosuppressants.
- The following words were used: ICI, immunosuppressant and irAE.
- Observational and clinical studies were included.
- A random effects model was used to estimate the overall incidence of infections associated to the treatment of these irAEs.



## Conclusion

- Adverse events from irAE treatment occurred in about one-third of patients that received steroids or any combination of steroids and other immunosuppressants.
- Consideration of shortening the treatment of irAE in those patients with risk factors.
- Larger studies are needed to further assess the safety of these medications in the context of patients with cancer.

| Author and Year | Infections | Study size | | Proportion [95% CI] |
|---|---|---|---|---|
| Alexander 2021 | 26 | 127 | | 0.20 [0.13, 0.27] |
| Au 2018 | 15 | 57 | | 0.26 [0.15, 0.38] |
| Beattie 2020 | 4 | 26 | | 0.15 [0.02, 0.29] |
| Johnson 2018 | 5 | 75 | | 0.07 [0.01, 0.12] |
| Kadokawa 2021 | 5 | 8 | | 0.62 [0.29, 0.96] |
| Li 2022 | 25 | 215 | | 0.12 [0.07, 0.16] |
| Shah 2022 | 22 | 112 | | 0.20 [0.12, 0.27] |
| Thompson 2021 | 17 | 50 | | 0.34 [0.21, 0.47] |
| Wang 2018 | 29 | 79 | | 0.37 [0.26, 0.47] |
| Zou 2021 | 44 | 184 | | 0.24 [0.18, 0.30] |
| Total (random effects model) | | | | 0.22 [0.15, 0.29] |

Percent of patients who had infections

## Results

- Eleven articles were included in the final review, they consisted from case series to clinical research, no clinical trials fitted our criteria.
- The most common irAEs were colitis followed by hepatitis.
- Virtually all the patients were treated with steroids and some with biologics.
- Infections were present in 22.3%, in some cases bacterial were the most commons although not fully described.

| Study information | | | Type of irAE | | Treatment for irAE | | | |
|---|---|---|---|---|---|---|---|---|
| First author and year | Patients n | GI n (%) | Hepatobiliary n (%) | Lung n (%) | Steroids n (%) | IFX n (%) | VDZ n (%) | Infection rate n (%) |
| Alexander 2021 | 127 | 127 (100) | 0 (0) | 0 (0) | 127 (100) | 127 (100) | 127 (100) | 26 (20.5) |
| Au 2018 | 57 | 0 (0) | 57 (100) | 0 (0) | 45 (78.9) | 0 (0) | 0 (0) | 15 (26.3) |
| Beattie 2020 | 26 | 0 (0) | 0 (0) | 26 (100) | 26 (100) | 20 (76.9) | 0 (0) | 4 (15.4) |
| Johnson 2018 | 75 | 75 (100) | 0 (0) | 0 (0) | 75 (100) | 36 (48) | 0 (0) | 2 (2.7) |
| Kadokawa 2021 | 8 | 7 (87.5) | 1 (12.5) | 0 (0) | 8 (100) | 8 (100) | 0 (0) | 4 (50) |
| Li 2022 | 215 | 55 (25.6) | 215 (100) | 58 (27.0) | 215 (100) | 0 (0) | 0 (0) | 25 (11.6) |
| Shah 2022 | 112 | 48 (42.9) | 28 (25) | 23 (20.5) | 112 (100) | 15 (13.4) | 3 (2.7) | 22 (19.6) |
| Thompson 2021[‡] | 50 | 0 (0) | 0 (0) | 0 (0) | 50 (100) | 0 (0) | 0 (0) | 17 (34) |
| Wang 2018 | 79 | 79 (100) | 0 (0) | 0 (0) | 79 (100) | 35 (44.3) | 0 (0) | 29 (36.7) |
| Williams 2019 | 103 | 0 (0) | 0 (0) | 28 (27.2) | 103 (100) | 0 (0) | 0 (0) | NR |
| Zou 2021 | 184 | 184 (100) | 0 (0) | 0 (0) | 184 (100) | 94 (51.1) | 63 (34.2) | 35 (19.0) |