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serious transaminase elevations (ALT, AST) and bilirubin were observed. Transaminase elevations occur early in the course of treatment (92.5% of all

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Review

June 18, 2013

## Risk of Infections Associated With mTOR Inhibitors

Br. J. Cancer 2013 Jun 04;[EPub Ahead of Print], MD Kaymakcalan, Y Je, G Sonpavde, M Galsky, PL Nguyen, DY Heng, CJ Richards, TK Choueiri



### ABSTRACT

**Background:** Mammalian target of rapamycin (mTOR) inhibitors are used in a variety of malignancies. Infections have been reported with these drugs. We performed an up-to-date meta-analysis to further characterise the risk of infections in cancer patients treated with these agents.

**Methods:** Pubmed and oncology conferences' proceedings were searched for studies from January 1966 to June 2012. Studies were limited to phase II and III randomised controlled trials (RCTs) of everolimus or temsirolimus reporting on cancer patients with adequate safety profiles. Summary incidences, relative risks (RRs), and 95% confidence intervals (CIs) were calculated.

**Results:** A total of 3180 patients were included. The incidence of all-grade and high-grade infections due to mTOR inhibitors was 33.1% (95% CI, 24.5–43.0%) and 5.6% (95% CI, 3.8–8.3%), respectively. Compared with controls, the RR of all-grade and high-grade infections due to mTOR inhibitors was 2.00 (95% CI, 1.76–2.28,  $P<0.001$ ) and 2.60 (95% CI, 1.54–4.41,  $P<0.001$ ), respectively. Subgroup analysis found no difference in incidences or risks between everolimus and temsirolimus or between different

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disease. Baseline and periodic monitoring electrocardiograms and maintenance of electrolytes within the normal range should be performed.

**Cardiac Dysfunction:** Cardiac dysfunction

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tumour types (renal cell carcinoma (RCC) vs non-RCC). Infections included respiratory tract (61.7%), genitourinary (29.4%), skin/soft tissue (4.2%), and others (4.9%).

**Conclusion:** Treatment with mTOR inhibitors is associated with a significant increase in risk of infections. Close monitoring for any signs of infections is warranted.

British Journal of Cancer

Risk of Infections in Renal Cell Carcinoma (RCC) and Non-RCC Patients Treated With Mammalian Target of Rapamycin Inhibitors

Br. J. Cancer 2013 Jun 04;[EPub Ahead of Print], MD Kaymakcalan, Y Je, G Sonpavde, M Galsky, PL Nguyen, DY Heng, CJ Richards, TK Choueiri

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