visceral crisis, for whom optimal management is still unclear: should these patients receive chemotherapy followed by CDK4/6 inhibitors plus endocrine therapy in maintenance, or should chemotherapy be continued until disease progression, or could endocrine and CDK4/6 inhibitor combinations also supplant chemotherapy for these patients? Ongoing studies will address the optimal management in this remaining small group of patients.

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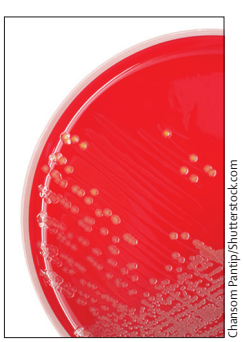
Reducing infection-related morbidity and mortality in patients with myeloma

Myeloma survival has substantially improved in the past 10 years.[1] Although most myeloma deaths are accountable to progressive disease, a substantial proportion of early deaths and deaths in remission are due to infections.[2] Febrile infections induce considerable morbidity and frequently lead to drug interruption or drug discontinuation. Drug discontinuation can lead to inferior treatment responses, translating to poorer survival outcomes.

Agents with new mechanisms of action and drug combinations dominate current clinical investigations in myeloma. We commend researchers for drawing our focus to an area of supportive care in myeloma. Myeloma is a disease of the elderly, with 40% of newly diagnosed patients in the UK older than 75 years. In their Article in *The Lancet Oncology*, Mark Drayson and colleagues[3] present findings that showed that 12 weeks of fixed-duration levofloxacin prophylaxis reduced the occurrence of febrile episodes and deaths (95 [19%] febrile episodes or deaths in 489 patients in the levofloxacin group *vs* 134 [27%] in 488 patients in the placebo group; hazard ratio [HR] 0·66, 95% CI 0·51–0·86; p=0·0018). Independent to levofloxacin, use of prophylactic low dose co-trimoxazole significantly reduced febrile infections and death. Additionally, use of levofloxacin for a fixed duration was not associated with an increase in adverse events; 597 serious adverse events were reported up to 16 weeks from the start of trial treatment—308 (52%) of which were in the levofloxacin group versus 289 (48%) in the placebo group).

The results of this trial[3] provide a good basis for considering fixed-duration quinolone prophylaxis for newly diagnosed patients with myeloma starting therapy, but several questions remain. Although the primary endpoint of the study was met, there were no differences in overall survival at end of 1 year.[3] This result could be partly explained by the high number of patients who had poorly controlled myeloma in this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See **Articles** page 1760

trial. Therefore, further trials are required to confirm this finding. There has been a switch to a continuous anti-myeloma therapy approach in newly diagnosed patients.[4] The risk for infections remains higher during the overall treatment period compared with time not receiving chemotherapy. Therefore, the duration of antibiotic prophylaxis might need to be extended to cover the ongoing risk of infection. Patients in this trial were primarily treated with immunomodulatory imide drug-based or proteasome inhibitor-based drug combinations,[3] but clinicians are moving towards monoclonal antibody-based drug combinations based on the results from the ALCYONE and MAIA studies.[5,6] Grade 3 and grade 4 infections were higher in the daratumumab group than in the non-daratumumab group in both studies. Whether the results from Drayson and colleagues' study can be extrapolated to chemotherapy treatment combinations is unclear. Moreover, it remains to be confirmed whether these results for newly diagnosed patients with myeloma can be generalised to patients with relapsed myeloma. Finally, co-trimoxazole was shown to have an independent effect on both febrile infections and death. The question remains as to whether a combination of both levofloxacin and co-trimoxazole should be recommended for patients on anti-myeloma therapy.

Data from the FIRST trial[7] provide criteria for identifying patients at high risk of grade 3 infection. These data have been validated in studies of patients with both relapsed and newly diagnosed myeloma. Therefore, patients who fit these criteria for high risk of grade 3 infection should be considered for antibiotic prophylaxis.

Use of antibiotics could increase antibiotic resistance and induce gut dysbiosis. Drayson and colleagues[3] showed that fixed 12-week levofloxacin prophylaxis does not result in increased carriage of *Clostridium difficile*, extended-spectrum β-lactamase Gram-negative coliforms, or meticillin-resistant *Staphylococcus aureus*. Whether carriage would increase if prophylaxis was extended for a longer period is unclear. Emerging data suggest a strong link between gut microbiota and host anti-tumour immunity.[8] Immunotherapies show great promise in relapsed myeloma. Longer-term antibiotic prophylaxis-induced dysbiosis has the potential to modify endogenous anti-tumour immunity and efficacy of immunotherapy in patients with myeloma.

Patients with myeloma have a high risk of viral infections. Therefore, other supportive measures to limit infections must be considered. Additional measures such as smoking cessation, infusion of intravenous immunoglobulins, pneumococcal vaccination, and seasonal influenza vaccination should also be contemplated. Data from a placebo-controlled, randomised study comparing two doses versus one dose of influenza vaccine showed higher antibody titres with two doses.[9] We await further data from this study as to whether higher antibody titres translate to clinical benefit.

Febrile infections lead to unplanned hospital admissions. Drayson and colleagues[3] report that health economic outcomes were collected in this study and we await these data.[3] A UK-wide study showed that emergency hospital admissions of patients with myeloma have higher health-care resource utilisation.[10]

In conclusion, this study is timely in showing that fixed-duration levofloxacin prophylaxis reduces febrile infections and early deaths in patients with myeloma during induction chemotherapy.[3] However, further trials are required in this area. In particular, assessment of the therapeutic effects of a combination of co-trimoxazole and levofloxacin and investigation of various durations of antibiotic prophylaxis are crucial to optimise patient outcomes.

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Cancer prevention and treatment in humanitarian settings: an urgent and unmet need

The WHO Eastern Mediterranean region is currently facing an immense burden of cancer. As well as being the site of numerous protracted crises, with over 50% of the region experiencing humanitarian emergencies, it is the WHO region that is expected to have the greatest increase in cancer incidence during the next 15 years.[1] Historically, humanitarian actors have focused on supporting conflict-affected populations through emergency aid and infectious disease prevention and treatment strategies. However, non-communicable diseases, including cancer, are increasingly prevalent in displaced and host populations in the Eastern Mediterranean region. Ageing, migration patterns, and associated sociocultural lifestyle changes, such as poor nutrition, tobacco consumption, and low levels of physical activity, have exacerbated exposure to cancer risk factors and have contributed to increasing cancer incidence.[2]

Despite the increasing burden of cancer, the global evidence base of peer-reviewed or grey literature surrounding cancer treatment and prevention in humanitarian contexts in the Eastern Mediterranean region is extremely scarce, and nearly all the available information on this topic comes from documentary sources and social media. Although research and response plans have grown to address both communicable and non-communicable diseases in these contexts, cancer treatment and prevention have seldom been addressed. In almost every recent humanitarian setting, the care of cancer patients and efforts dedicated towards cancer prevention have been neglected because of local and global political and economic determinants, such as legal status, freedom of movement, affordable treatment, and availability of health resources and research. Similarly, the delivery of health care through humanitarian systems is often parallel to and not well integrated with the health systems of host nations, which further complicates the provision of cancer treatment services.


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Although both the WHO Constitution and the 1948 Universal Declaration of Human Rights reinforce a global commitment to preserving access to health care as a basic human right, which extends to the provision of cancer screening, diagnosis, and treatment services, the inaccessibility of cancer care has been well documented across humanitarian settings in the Eastern Mediterranean region.[1] Lebanon hosts more than 1 million Syrian refugees, 74% of whom do not have legal status. Given the country's highly privatised and fragmented health system, these individuals do not have access to any form of public health insurance and must finance the cost of treatments on their own.[3] Based on the Lebanese Ministry of Public Health's utilisation and spending data, the annual average cost of cancer drug treatment, which does not include radiotherapy, is US$6475 per patient, and Syrian refugee families have been reported to earn an average monthly income of less than $300.[4,5] In Jordan, nearly 900 Syrian refugees are diagnosed with cancer annually and have no sustainable access to affordable treatment, with the cost of treating this growing population exceeding $22 million; in addition, Syrian refugees in Jordan are required to pay 80% of the amount that is paid by foreigners without insurance, which imposes a large financial burden on refugee families.[6] In both Lebanon and Jordan, refugees have few treatment-seeking options due to an inability to move freely within or across countries, not having proper documentation as a result of forced migration, and the fear of detainment