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Palifermin in Myelotoxic Therapy-Induced Oral Mucositis

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Oral mucositis is among the most common toxicities of many of the myeloablative regimens used for conditioning prior to haematopoietic stem cell transplantation (HSCT). The pain caused by mucositis is so significant as to result in it being the most frequently mentioned adverse effect of treatment by patients. In addition, the loss of an intact epithelial barrier in an environment so microbiologically rich as is the mouth results in lesions of mucositis serving as portals of entry for systemic bacterial invasion. In fact, the mouth is the most frequently identifiable site of origin of bacteraemias in granulocytopenic cancer patients. As a consequence, patients with mucositis have more days of opioid and antibacterial use, and more days of fever and use of total parenteral nutrition, than do patients without the condition. Economically, mucositis results in prolonged, expensive hospital stays.

The pathobiology of mucositis is more complex than has been described historically. While direct clonogenic cell death of epithelial basal cells plays a role in mucositis development, it has been increasingly clear that the condition represents the culmination of a cascade of biological events that involve all of the tissues and cells of the submucosa. Included in this cascade are transcription factors, cytokines and mediator proteins.

Until recently, treatment of mucositis was limited to palliative agents or systemic analgesics. Palifermin is the first approved agent that effectively modulates the course and duration of the condition. Importantly, it confirms the concept that an effective intervention is one which is mechanistically based and has biological pleiotrophism directed at multiple pathways involved in mucositis pathogenesis. While palifermin is often thought of principally as a stimulator of epithelial proliferation, its activities related to the activation of specific transcription factors to upregulate detoxifying enzymes and attenuate proinflammatory cytokine production likely contribute to its efficacy against mucositis. Likewise, its cytoprotective activities relating to DNA strand breaks and inhibition of apoptosis are likely to contribute to its efficacy.

Mucositis patients among HSCT recipients represent <5% of the total population who develop the condition each year. The approval of the first agent to effectively treat the condition thus represents an important proof of concept and, perhaps more significantly, provides hope that additional cohorts of cancer patients will no longer have to suffer the burdens caused by mucositis. ▲