Title: Optimizing Radiation Therapy: Novel Radioprotective Agents

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Aims and Scope:

Radiotherapy, both by external radiation (X-ray, γ-ray etc.) and/or targeted radionuclide therapy, is the most common modality for treating human cancers. Eighty to ninety percent of cancer patients undergo radiotherapy sooner or later, either for curative or palliative purposes. In order to achieve optimum therapeutic success a reasonable balance between the total dose of radiotherapy delivered to the tumor and the threshold limit of the surrounding normal critical tissues is required. To keep this balance targeted adjuvant radioprotective therapy is an essential tool. Research on radioprotection has unraveled some basic mechanisms and yielded a large number of radioprotecting compounds, majorily, sulfhydryl compounds, water-soluble nitroxides and other antioxidants like amifostine, tempol or melatonin. Other approaches used stimulators of tissue recovery and regeneration, compounds showing immunomodulatory properties, and absorbents. However, most of the compounds failed in their transition from experimental study to clinic. Acute toxicity, unsuitable way of administration, insufficient window of action/protection and their non-targeted mode of action, comprising inability to differentiate between tumor and normal cells are main reasons for limited clinical applications. To avoid this, some recent approaches used established drugs like hydroxymethylglutaryl-coenzyme A (HMG-CoA) reductase inhibitors (statins), angiotensin-converting enzyme (ACE) inhibitors and angiotensin II type-I receptor blockers. The literature on radioprotecting agents is enormous, but more recently discussion focuses on targeted radioprotectors, depending on their molecular structure, therapeutic activity or metabolic function. Particularly, compounds targeting mechanisms of low-dose radiation-induced site-specific normal tissue injury are under discussion.

Among them are local pathologies, like injury of the gastrointestinal tract or the brain, and more systemic effects, like injury of hematopoietic system or radiation-induced vascular dysfunction. The latter is of specific importance because radiation has been identified as an independent risk factor in accelerated vascular disease and, therefore, is a major dose limiting factor in radiotherapy. In these themed issue the development characterization novel synthetic (e.g., nitroxide compounds, benzothiazoles, indole derivatives) and various natural compounds (e.g., polyphenols) with high potential for targeted radioprotection and radiomitigation during cancer radiotherapy will be discussed.