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Phase 1/2a, dose-escalation, safety, pharmacokinetic and preliminary efficacy study of intratumoral administration of BC-819 in patients with unresectable pancreatic cancer.

Hanna N, Ohana P, Konikoff FM, Leichtmann G, ..., Appelbaum L, Kopelman Y, Czerniak A, Hochberg A 
Cancer Gene Ther. 2012 Jun; 19(6):374-81

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John Nemunaitis, Mary Crowley Medical Research Center, TX, USA. F1000
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Hanna et al. describe a novel DNA plasmid (called BC-819) that enables expression of the diphtheria-toxin gene under the control of the H19-directed promoter, clinically tested in the management of local regional pancreatic cancer that is unresectable. This population of patients has a less than 20% chance of five-year survival under optimal circumstances which involves conversion to surgical resectability. Without surgical resection chances of living 5 years are virtually zero. This plasmid-based technology is unique in that it demonstrates tumor-specific targeting through use of a regulatory promoter dependent on tumor-exclusive expression of H19 transcription factors. Local injection of 4 and 8mg of plasmid revealed local regional safety to the product. Moreover, transient circulating levels of plasmid at levels up to 722,603 copies per μ l of blood was not associated with any clinically relevant toxic effect in any of the patients (8 tested/8 demonstrated circulating plasmid). Three out of nine patients (all at the 8mg dose) demonstrated partial response at month three (one received radiation/gemcitabine after study treatment). Two of these partial response patients later were determined to be surgically resectable and underwent surgical resection.

There are two issues worth pointing out further with this manuscript. (1) Not highlighted is the remarkable coordination between the University of Maryland School of Medicine and Israeli treatment centers (Meir Medical Center; Sheba Medical Center; Hadassah Medical Center; and Hillel Yaffe Medical Center). Trials of this sort with Food and Drug Administration (FDA), Israeli and NIH regulatory hurdles are very difficult to coordinate, particularly with outsourced GMP (Good Manufacturing Practice) product manufacturing as was done by Althea Technologies, Inc., San Diego, California, under sponsorship by BioCancell Therapeutics Ltd., Israel. (2) Clinical benefit with safety appears to be demonstrated with local regional management. Potential utilization of a systemic delivery vehicle may be a future next step in further development of BC-819. Systemic safety with circulating plasmid appears to justify such an approach.

Competing interests

None declared

 [Cite this evaluation](#)

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Short form

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