

ORAL PRESENTATIONS

NANOMEDICINE FOR EFFICIENT CHEMOTHERAPY OF BRAIN TUMOURS: FROM BENCH TO BEDSIDE

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Brain tumours, particularly glioblastomas, are among the most aggressive human cancers and remain associated with a very poor prognosis. Current treatment relies mainly on neurosurgery and radiotherapy, whereas the contribution of chemotherapy remains limited, largely because most anticancer drugs penetrate the blood–brain barrier (BBB) poorly. For example, the limited brain distribution of doxorubicin (DOX) is considered one of the main reasons why this potent antitumour antibiotic has not been successfully used for glioblastoma chemotherapy.

The nanoparticle formulation of doxorubicin (DOX-PLGA) was developed as a novel candidate for systemic chemotherapy of glioblastoma. The technology is based on poly(lactide-co-glycolide) (PLGA) nanoparticles coated with poloxamer 188. Following intravenous administration, the nanoparticles acquire a biological surface through adsorption of plasma proteins, including apolipoproteins, which is believed to contribute to their altered biodistribution and improved delivery of doxorubicin to brain tumours. Recent evidence further suggests that interactions with blood cells, particularly erythrocytes, may also contribute to the altered biodistribution of nanoparticles, although the underlying mechanisms remain to be fully elucidated.

Preclinical studies demonstrated that DOX-PLGA produced pronounced growth inhibition of intracranially implanted 101.8 glioblastoma in rats and induced long-term remission in more than 20% of animals, whereas the conventional formulation was only marginally effective. Histological examination confirmed the antitumour effect and demonstrated efficient intratumoral penetration and accumulation of the nanoparticles. Importantly, DOX-PLGA also exhibited a favourable toxicological profile, particularly with respect to cardiotoxicity, as demonstrated by both functional and histological evaluation. The reduced toxicity is most likely associated with nanoparticle-mediated changes in drug biodistribution.

The laboratory manufacturing process was successfully optimized, scaled up and transferred to pilot production.

A Phase I dose-escalation clinical study of DOX-PLGA in patients with advanced solid tumours (including glioblastoma), sponsored by Drugs Technology Ltd., is currently ongoing in Russia. The formulation has been well tolerated and no dose-limiting toxicity has been observed at the dose levels investigated so far (up to 60 mg/m²).

Overall, this work demonstrates the potential of PLGA-based nanomedicine to improve the therapeutic index of doxorubicin and illustrates the successful translation of a laboratory-developed drug delivery system from preclinical studies towards clinical evaluation.