Physiomics’ Virtual Tumour technology

Physiomics’ key technology is Virtual Tumour, which provides a platform for identifying, ranking and optimizing anti-cancer treatments, and in particular combination regimens [1,2]. Virtual Tumour (Figure 1) is a computer model that simulates tumour cell division and the effect of antineoplastic agents, taking into consideration the differences between proliferative cells and those that are part of the necrotic core. The complexity of the model is deliberately constrained so that it can be parameterized with data that are usually produced during drug development. These data include PK data for the drug, biomarkers showing the cell population response, and growth measurements showing how tumour growth is affected. This technology provides a rationale for designing an appropriate schedule, and allows our partners to prioritize the most effective drug combinations.

Aims and objectives

We have previously developed models that replicate and predict the effect that radiation therapy (RT) has on tumour growth inhibition in several preclinical studies. These studies involve different RT doses and regimens as well as combinations with therapeutic agents with disparate mechanism of action. These encouraging results in the preclinical space led us to develop an enhanced strategy for modelling RT treatments using a tumour model that can predict tumour shrinkage and long-term regrowth in a clinical setting (squamous cell carcinoma of the head and neck).

Data sets

• Phase 3 randomized trial of concomitant radiotherapy and cisplatin in patients with advanced head and neck cancer. A dose of 70 Gy in 35 fractions over 7 weeks was delivered while cisplatin (100 mg/m²) was administered over 1 hour on day 1 of weeks 1, 4 and 7. (ClinicalTrials.gov Identifier: NCT00094081) [3]

• Phase 3 randomized study of cisplatin in patients with recurrent or metastatic head and neck cancer. A dose of cisplatin (75 mg/m²) was administered on day 1 every 21. (ClinicalTrials.gov Identifier: NCT00415194) [4]

Characterisation of clinical head and neck tumour dynamics

• The initial rate of SLD (sum of longest diameter) shrinkage depends on the SLD before treatment. The tumour with the largest initial SLD shows the fastest initial tumour shrinkage rate (Figure 2 and 3).

• The magnitude of the tumour shrinkage can not be explained only by depletion of proliferative layer of the tumour.

• Many tumours remained suppressed for several years and a wide range of times to regrowth were observed (Figure 3).

Virtual Tumour clinical model for cisplatin

The initial rate of SLD (sum of longest diameter) shrinkage depends on the SLD before treatment. The tumour with the largest initial SLD shows the fastest initial tumour shrinkage rate (Figure 2 and 3).

Virtual Tumour clinical model for RT & cisplatin

Radiation (RT) mode of action. It damages DNA in all phases.

Conclusions

Starting with a model that explained and predicted the effect of cisplatin/radiotherapy on tumour growth inhibition in the preclinical space we were able to extend it to one that describes both tumour growth inhibition and regrowth in the clinical space. Thus, we have developed a platform for head and neck cancer that could be used to predict the effects of radiotherapy alone or in combination with other procedures on tumour shrinkage and locoregional control. This approach can also be implemented to model other tumour types.