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Kevin Atsou, Anne Auperin, Joël Guigay, Sébastien Salas, Sébastien Benzekry. Machine Learning and Mechanistic Modeling for the prediction of Overall Survival on the basis of 1st line Tumor Dynamics in Head and Neck Squamous Cell Carcinoma. Colloque Science numériques et intelligence Artificielle pour la Santé, AMU, Nov 2021, Marseille, France. hal-03467230

HAL Id: hal-03467230
https://inria.hal.science/hal-03467230
Submitted on 6 Dec 2021

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Machine Learning and Mechanistic Modeling for the prediction of Overall Survival on the basis of 1st line Tumor Dynamics in HNSCC

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BACKGROUND

- Prediction of Overall Survival and Response to 2nd line is a major challenge in treatment of HNSCC
- Tumor kinetics during first line may provide interesting predictive metrics for Overall Survival

OBJECTIVES

- Propose the best mathematical model for the description of the longitudinal measurement of the patients individual SLDs
- Predict the Overall Survival using the kinetic data of first line and some baseline data

MATERIAL AND METHODS

Clinical data

- EXTREME (cetuximab, 5-FU, platinum) vs TPEx (cetuximab, docetaxel, platinum)
- Phase 2 clinical trial
- 528 patients enrolled (263 (TPEx) and 265 (EXTREME))

Tumor Growth Inhibition (TGI) models:

- Tumor Growth model with treatment effect
- Biexponential model with resistant cells
- Biexponential model

Nonlinear Mixed Effects Modeling (NLMEM)

\[ SLD(t) = SLD_0 e^{-\frac{1}{\lambda}} e^{-\frac{1}{\lambda_b t}} \]

RESULTS

The Biexponential model provides the best Fit (AIC and identifiability)

- Best performance for Random Survival Forest (C-index= 0.7)
- KG is the most important parameter for predicting OS

CONCLUSION AND PERSPECTIVES

- A mechanistic mathematical model was able to fit the clinical data of SLD measurements in a HNSCC clinical trial
- Mechanistic modeling and Machine learning algorithms were combined to predict Overall Survival
- Predictive power is only modest so far but only the SLD measurements was considered
  => include more features and model individual lesions kinetics

References

1. S. Benzekry, Artificial Intelligence and Mechanistic Modeling for clinical Decision Making in Oncology, Clinical Pharmacology and Therapeutics (2020)