OPTIMAL TIMING OF PANITUMAB-IRDYE800CW ADMINISTRATION FOR SURGICAL FLUORESCENCE IMAGING FOR HEAD AND NECK CANCER

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ABSTRACT

Introduction

Surgical fluorescence imaging with EGFR targeting antibodies, including panitumumab-IRDye800CW (Pan800), has been previously demonstrated to identify cancer in real time. In this study, we evaluate the optimal timing of administration of Pan800 prior to surgery.

Method

We evaluated 17 patients who received a 50mg dose of Pan800 administered 2-7 days preoperatively prior to head and neck cancer surgery (NCT #05945875, #04511078). Quantitative and qualitative assessment of fluorescent intensity was performed on plasma and tumor tissues to correlate the concentration of Pan800 relative to the timing between infusion and surgery. In addition, paraffin blocks from the primary site were pathologically divided into tumor-positive and tumor-negative blocks to evaluate mean fluorescence intensity (MFI) as a surrogate for drug signal.

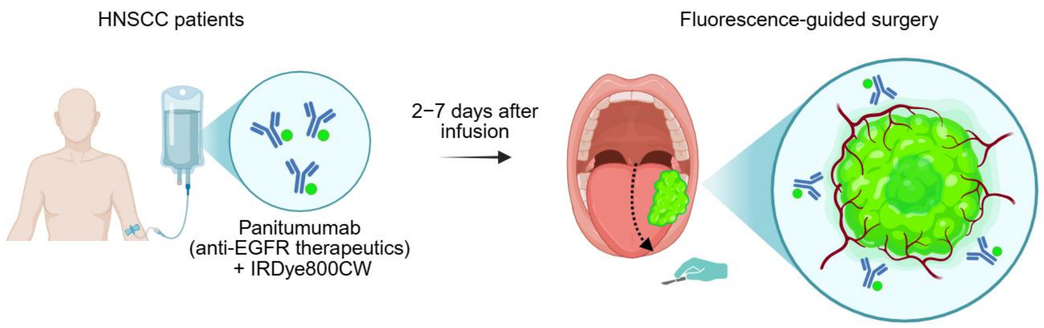
Result

Pan800 concentrations in fresh samples negatively correlated with the time from infusion to surgery in both plasma ($t_{1/2}$=34hours) and tissue ($t_{1/2}$=27hours). The percentage of intact Pan800 based on SDS-PAGE also negatively correlated with time in both plasma ($t_{1/2}$=28hours) and tissues ($t_{1/2}$=59hours). The median MFI of malignant blocks was significantly higher on day 2-3 compared to day 4-7. However, the tumor-to-background ratio (TBR), calculated by dividing the MFI of the tumor-positive blocks by the MFI of tumor-negative blocks, did not change over time.

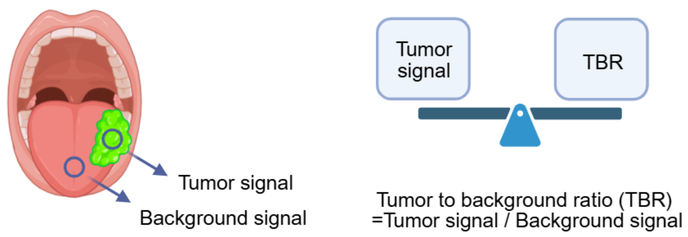
Conclusion

The intensity of the Pan800 signal degrades in both plasma and tissues after 3 days. The optimal timing for surgical imaging using antibody-based fluorophores is likely within 3 days.

SURGICAL FLUORESCENCE IMAGING

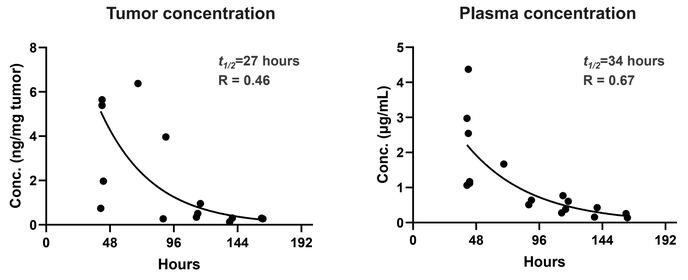


THE FACTORS THAT AFFECT SURGICAL IMAGING



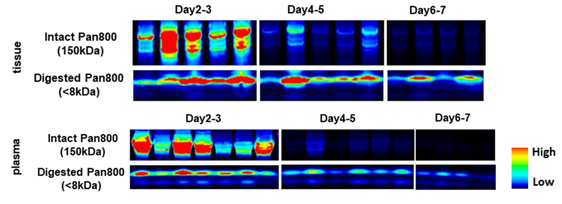
The goal of this study = To identify the optimal timing for surgery after infusion

PAN800 CONCENTRATION IN TISSUE AND PLASMA

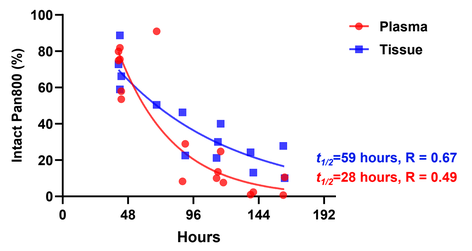


The concentration of Pan800 in frozen tissues and plasma was measured using a fluorescence plate reader. Frozen tissues were homogenized in lysis buffer prior to measurement. The relationship between Pan800 concentration and time was visualized by fitting the data to a one-phase decay model. In both tumor tissues and plasma, Pan800 levels decreased over time.

PAN800 DEGRADATION IN TISSUE AND PLASMA

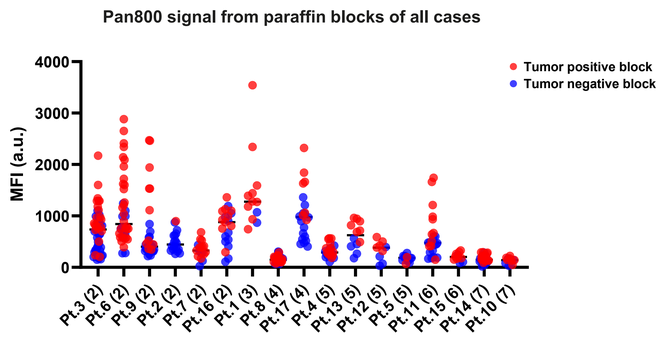


To evaluate the degradation of Pan800, tissue lysates obtained from frozen tissues and plasma were applied to a gel and subjected to SDS-PAGE.

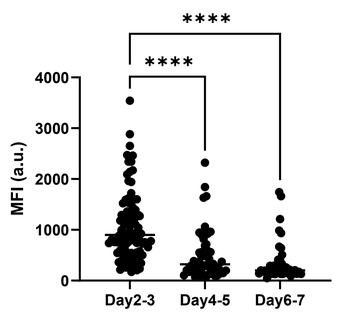


The percentage of intact Pan800 relative to the total Pan800 was calculated based on the signal intensities obtained from SDS-PAGE. These values were then fitted to a one-phase decay model to visualize the relationship between degradation and time. The results revealed that Pan800 undergoes degradation in both tissue and plasma.

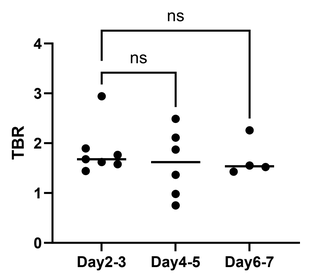
PAN800 SIGNALS IN PARAFFIN BLOCKS



Signals from paraffin blocks obtained from primary tumor resections were acquired using the Odyssey CLx fluorescence scanner. Based on H&E findings, each block was classified as either containing tumor cells or not. For each patient, the mean fluorescence intensity (MFI) of each block was visualized. The numbers in parentheses indicate the number of days between Pan800 administration and surgery.



The signal from paraffin blocks positive for tumor cells was significantly higher on days 2–3. Statistical significance was assessed using Dunn's multiple comparisons test.



For each case, the tumor-to-background ratio (TBR) was calculated by dividing the average MFI of tumor-positive blocks by that of tumor-negative blocks. Within the range of days 2 to 7, no significant time-dependent changes in TBR were observed. Statistical significance was assessed using Dunn's multiple comparisons test.

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