11 days for samples reconstituted by 4ºC water and 7 days for those reconstituted by 25ºC water. To evaluate how freezing can affect the physical stability, we studied the characteristics of the suspension before and after freezing (−20ºC, 48 hours) and thawing at room temperature. The sedimentation kinetics was studied by following the decrease of absorbance at 500 nm versus time. The aspect of crystals, after filtration on a 0.22 μm filter, was studied by scanning electron microscopy.
Results: The degradation of AZC followed a biphasic kinetic with a rapid initial phase strongly depending on the temperature (% of remaining AZC at 25ºC: 93.2%; 4ºC: 95.9%). Using water at 25ºC, the rate of initial degradation is higher than using cold water (0.336% hr^{-1} vs 0.162% hr^{-1}). However, regardless of the initial conditions of reconstitution, the total degradation was less than 5% after 7 days if reconstituted vial was immediately stored at 4ºC. After storage at −20ºC, no degradation of AZC was observed. The physical characteristics of suspension were not modified: sedimentation rate (4ºC: 144 s; −20ºC: 152 s); identical size and shape of crystals.
Conclusion: If syringes are stored at 4ºC immediately after reconstitution, the use of iced water permits only to slow the initial degradation step but is not essential since the total degradation remains inferior to 5% after 7 days for both reconstitution temperatures. Therefore, the in-use stability period of AZC suspension is higher than recommended by the manufacturer. Freezing should permit long term storage of the suspension without any physical and chemical alterations.

Poster Discussion Presentations (Mon, 26 Sep, 08:00−09:00)

Biomarkers / Imaging

1400 POSTER DISCUSSION

Interest of CHOI and Modified CHOI Criterion for Evaluation of Metastatic Renal Cell Carcinomas (mRCC) Patients Treated With Everolimus

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Background: Because tumour response may be underestimated by RECIST as new targeted therapies can induce more necrosis than tumour shrinkage, we studied whether CHOI and modified CHOI (mCHOI) criterion might be valuable to assess everolimus efficacy.
Materials and Methods: We, retrospectively, reviewed the computed tomography (CT) of 70 mRCC patients (pts) enrolled in the French centers participating to the randomized, double-blind, multicenter phase III study comparing Everolimus vs placebo (RECORD-1). In this trial, the primary endpoint was PFS, based on RECIST criteria assessed on CT performed at baseline and every two months. We investigated CT until first progression according to CHOI criteria where partial response (PR) was defined as $\geqslant$10% decrease in tumour size OR $\geqslant$15% decrease in attenuation; and according to mCHOI criteria where partial response (PR) was defined as $\geqslant$10% decrease in tumour size AND $\geqslant$15% decrease in attenuation. Attenuation was measured on region of interest covering at least $\frac{3}{4}$ of the surface area of the targeted lesions on the CT sections where the largest diameter could be measured.
Results: Because of renal impairment that precluded contrast injection and lesions that could not correctly be assessed for attenuation, only 50 pts were eligible for analysis. Among them 19 were in the placebo arm and 31 treated by Everolimus. PFS were 2.8 and 6 months ($p < 0.005$), respectively. In the placebo group, CHOI criteria identified 47% of PR compared to non-responders with significant differences for PFS (3.6 vs 2.0 months $p < 0.01$, respectively), while mCHOI criteria found 0% of PR.
In the Everolimus group, 55% of pts were considered PR and 45% non responders according to CHOI criteria without significant differences for PFS (6.0 and 5.9 months, respectively) while mCHOI found 26% PR compared to 74% non-responders without significant differences for PFS (7.4 and 5.5 months, $p = 0.13$, respectively).
Conclusion: The use of CHOI or mCHOI criterion could not discriminate PFS between responders or non-responders pts treated with Everolimus. In the placebo arm, CHOI criteria identified a subgroup of pts with spontaneous necrosis associated with a longer PFS.

1401 POSTER DISCUSSION

Choi Response Criteria for Prediction of Clinical Outcome in Patients With Metastatic Renal Cell Carcinoma Treated With Targeted Therapies

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Background: Anticancer treatment efficacy is measured by decrease in tumour size and standardized according to the Response Evaluation Criteria in Solid Tumours (RECIST). With the advent of new targeted therapies, necrosis and cavitation rather than shrinkage were described as first response to treatment. The purpose was to evaluate whether early assessment of tumour shrinkage alone (RECIST criteria) or combined with changes in tumour density (Choi criteria) better predict clinical outcome in patients with metastatic renal cell cancer (mRCC).
Patients & Methods: In this retrospective multicenter study we included 47 patients with mRCC treated with a tyrosine kinase and/or mTor inhibitor and for whom at least two CT scans (baseline and follow-up) with measurable lesions were available. CT scans were blinded and analyzed centrally according to RECIST and Choi criteria. Patients were categorized according to both criteria into complete and partial response (CR/PR), stable disease (SD) and progressive disease (PD). A dichotomisation into responders (CR or PR) and non-responders (SD or PD) was conducted. The response to therapy was compared with clinical outcome including progression free survival (PFS) and overall survival (OS). Differences in survival of responders and non-responders were assessed with log-rank tests and Cox proportional hazards models.
Results: According to RECIST criteria, 8 patients were responders and 26 patients non-responders, whereas to Choi criteria, 17 were responders and 17 non-responders.
Responders had higher PFS and OS according to Choi criteria (log-rank test $p = 0.001$ and $p = 0.023$, respectively) than according to RECIST criteria ($p = 0.404$ and $p = 0.055$, respectively). Based on Cox proportional hazards models adjusted with prior treatment with interferon and the time between diagnosis and start of therapy, the hazard ratios for responders vs. non-responders according to Choi criteria were 0.25 for PFS (95% CI 0.10–0.61, $p = 0.002$) and 0.33 for OS (95% CI 0.12–0.90, $p = 0.030$) as opposed to the hazard ratios according to RECIST criteria of 0.59 for PFS (95% CI 0.21–1.65, $p = 0.313$) and 0.34 for OS (95% CI 0.10–1.17, $p = 0.087$).
Conclusion: Using Choi criteria in evaluating mRCC patients treated with targeted therapies will change response evaluation and better correlates with PFS and OS compared to using RECIST criteria.

1402 POSTER DISCUSSION

CT Evaluation of the Response of Colorectal Liver Metastasis After Bevacizumab Treatment − a Density Quantitative Analysis Correlated With Patient Outcome

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Context: The standard criteria used to evaluate tumour response, the Response Evaluation Criteria in Solid Tumours (RECIST), were developed to assess tumour shrinkage after cytotoxic chemotherapy and may be limited (1) in assessing response to biologic agents, which have a cytostatic mechanism of action.
Purpose: To validate novel tumour response criteria based on tumour size and density early changes observed on computed tomography (CT) in patients with colorectal liver metastases treated with bevacizumab-containing chemotherapy regimens.
Material and Methods: We performed a centralized review of the 145 patients included in ACCORD 13 prospective clinical trial (NCT00423696). Seventy one patients were excluded of the analysis because of the absence of liver metastasis (n = 19), images data not available or incomplete (n = 30), CT delay time not respected (n = 7), CT acquisition protocol not respected (n = 15). The final study population was 74 patients treated by FOLFIRI + Bevacizumab (n = 46) or XELIRI + Bevacizumab (n = 28), with a median follow up of 34.1 months [2.8–47.5 months]. Tumour size (RECIST) and density were determined objectively using a semi- automatic segmentation tools (Myran®, Intrasense) at the portal phase. We analyzed changes in tumour size and density, in patient who underwent a CT scan before and 2 months after starting treatment.
Results: There was no significant difference between the entire clinical trial population study (ACCORD 13) and the analysed patient group in terms of age, sex, PFS and OS. The RECIST response (PR or CR)