The presence of FDG-PET/CT focal, not osteolytic, lesion(s) identifies a sub-group of patients with smoldering multiple myeloma with high risk of progression into symptomatic disease

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Background

- Smoldering multiple myeloma (SMM) has an high variable risk of progression to symptomatic disease (MM).
- Several biological and imaging markers have already been established to identify sub-groups of SMM patients with a highest risk of progression into MM.
- FDG-PET/CT is a reliable technique for assessing early skeletal involvement and for predicting outcomes at the onset of MM.
- However, no data are available regarding the impact of PET/CT in SMM on time to progression into MM.

Methods

- To address this issue, we prospectively studied pts with a suspected diagnosis of SMM with FDG-PET/CT.
- A cohort of 73 pts, with a median age of 61 years old (range 27-83) and a confirmed diagnosis of SMM, were followed for a median of 2.2 years.
- By study design, all the pts were studied with PET/CT at baseline. The number, the size and the associated standardized uptake values (SUV) of each FL were recorded.
- Pts with underlying osteolytic lesions associated to FLs were excluded as they were considered as having symptomatic MM.
- Three-four monthly laboratory follow-up plus MRI and PET/CT at occurrence of symptoms or an increase in M component were planned.
- Progression to MM was defined by the presence of CRAB features. Skeletal progression was defined by the appearance osteolytic bone lesions, pathological fractures and/or soft masses at PET/CT or MRI. The start of systemic therapy was defined as the date of progression into MM.

Results

- Clinical baseline patient characteristics were reported in enclosed Table.
- Baseline PET/CT was positive in 9/73 (12%) of patients; 5 pts had 1 FLs (56%), 1 pt 2 FLs, 2 pts ≥3 FLs and 1 pt a diffuse BM involvement. Median SUV max value was 4.45 (range 2.5-5.2).
- Serum and urine baseline characteristics were not significantly different between patients with positive or negative PET/CT.
- 37% of the pts progressed to MM in a 4 years median time, including 21% with skeleton involvement, with/without the appearance of other CRAB symptoms, and 16% with exclusive serological signs of progression.
- 66% of pts with positive PET/CT progressed to MM in comparison to 33% of the pts with negative PET/CT (P = 0.034).
- The relative risk of progression of the pts with a positive PET/CT was 2.3 (95% CI 0.9-5.9, P = 0.06).
- Moreover, the relative risk of skeletal progression was 4.0 (95% CI 1.3-12, P= 0.013), with a median TTP of 2 yrs for pts with positive PET/CT vs 7 yrs for those with negative PET/CT (Figure).

Conclusions

Approximately 10% of the pts with SMM have a positive PET/CT, mainly with few FLs, without underlying osteolytic lesion, with a low FDG uptake and with clinical baseline characteristics superimposable to the entire sample.

PET/CT positivity significantly increased the risk of progression of SMM into active MM; the probability of progression of PET positive patients at 3 years was 65%.

In conclusion, PET/CT could become a new risk factor to define a high risk set of SMM pts. Further studies are needed to find an optimal cut off point of FLs to capture the higher risk of progression at 2 years and to construct a risk score with other prognostic factors.