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JOURNAL CLUB

Article Summary by: Matthew Koslow, MD and Ayodeji Adegunsoye MD, MS, FCCP

ARTICLE

Leukocyte telomere length and mycophenolate therapy in chronic hypersensitivity pneumonitis. *Eur Respir J* 2021; 57: 2002872

CLINICAL QUESTION

Are patients with chronic hypersensitivity pneumonitis and short telomere length (TL) at increased risk for mortality and disease progression when compared to those with longer TL?

SUMMARY

Patients with pulmonary fibrosis and short telomere syndrome may be at increased risk for adverse outcomes when exposed to immunosuppression regardless of their ILD diagnosis. Since many patients with progressive non-IPF forms of interstitial lung disease are prescribed immunosuppression, they may be harmed when exposed to such treatment. The authors of this work sought to determine whether patients with chronic hypersensitivity pneumonitis (HP) and short telomere length (TL) would experience increased mortality and disease progression when exposed to mycophenolate mofetil compared to those with longer TL. After excluding those exposed to azathioprine, the study population included 189 patients with a confident diagnosis of HP from four academic centers. Baseline characteristics are shown below (author figure a). TL measurement was performed using quantitative PCR from peripheral blood leukocytes, age-adjusted using normal controls and categorized into quartiles.

Patients were categorized based on MMF therapy >500mg per for at least one month with propensity score adjustment for variables likely associated with MMF treatment. Baseline characteristics are shown below. Median MMF exposure time was similar for patients with TL in the first quartile (Q1) and those in the second to fourth quartiles. Use of corticosteroids was also similar between both groups. Baseline FVC was lower in Q1 patients that received MMF (63.2%±18.2% vs 74.1±14.7%, p=0.029) whereas baseline DLco was lower in Q2-Q4 patients who received MMF (48.2% ±20.3% vs 58.2±24.4%, p=0.011).

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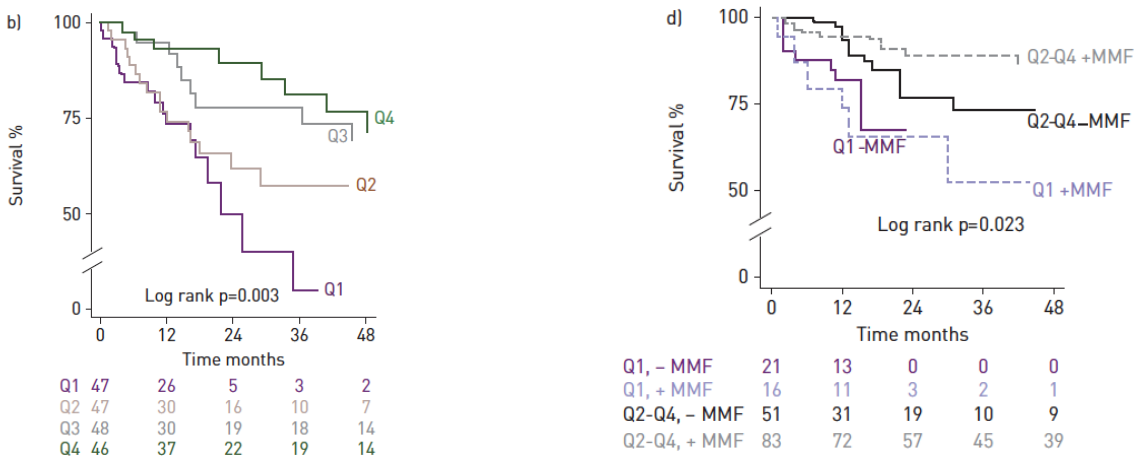
a)

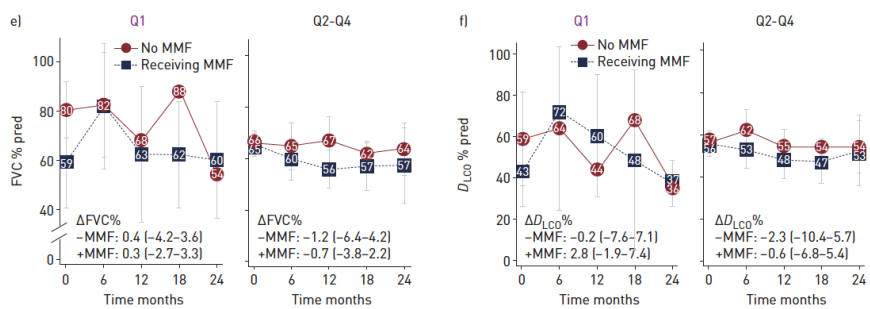
Parameter	UCHICAGO (n=78)	UCDAVIS (n=49)	UCSF (n=35)	UTSW (n=27)
Age years	65±9	71±10	60±11	62±9
Male	39 (50)	23 (47)	14 (40)	16 (59)
White	66 (85)	40 (82)	30 (86)	24 (89)
Tobacco pack-years	16±24	11±18	17±13	16±27
Env. antigen	24 (31)	49 (100)	35 (100)	21 (78)
FVC %	65±20	66±20	71±15	59±19
D_{LCO} %	55±25	52±24	58±13	45±19
Surgical biopsy	43 (55)	15 (31)	25 (71)	16 (59)
Corticosteroid	54 (69)	38 (78)	26 (74)	24 (89)

RESULTS

Each quartile decrease in TL was associated with a decrease in transplant-free survival (author figure b). Q1 patients had increased mortality compared to Q2-Q4 which remained significant after propensity score adjustment. Survival was improved for Q2-Q4 patients who received MMF but not for Q2-Q4 without MMF nor Q1 irrespective of MMF therapy (author figure d).



Notably, the annual change in FVC and DLco did not differ with MMF regardless of the TL.



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GROUP OPINION

The results of this study support the previous investigations that patients with fibrosing ILDs and short telomere length may have worse outcomes when exposed to immunosuppression. Although this may not change management of IPF, many patients with progressive non-IPF forms of ILD are still exposed to immunosuppression. If the pharmacogenetic interaction between telomere length and immunosuppression persists regardless of ILD diagnosis, then such patients may be harmed. These results highlight the potential role to tailor management of patients with non-IPF diagnoses more precisely based on telomere length.

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