Analysis of mortality in patients with giant cell arteritis presenting with isolated inflammation or fever of unknown origin

Sirs,

We read with great interest the letter by Dr Gilutz (1) related to our article published in *Clinical and Experimental Rheumatology* (2). This letter emphasised the higher mortality rate of patients with giant cell arteritis (GCA) presenting with isolated inflammation or fever of unknown origin (IFUO) when compared to the other patterns of GCA (2). In this previous work, we aimed to describe the different clinical patterns of GCA at diagnosis in a well-defined population of 693 patients with GCA demonstrated on biopsy or imaging. We identified four patterns at diagnosis: isolated cranial GCA (affecting 80% of patients), GCA with symptomatic large-vessel vasculitis (9%), GCA presenting with IFUO (9%), and patients with isolated polymyalgia rheumatica and vasculitis demonstration (2%).

Dr Gilutz provided a careful and very interesting analysis of death rates in each group and calculated the annual mortality rate using the follow-up time. Given the shorter follow-up time of patients with IFUO (28 [0-139] months, *versus* 50 [0–279] months and 76 [0–264] months in patients with isolated cranial GCA and GCA patients with symptomatic large-vessel vasculitis, respectively), he found a higher annual mortality rate in patients with IFUO. In another detailed analysis we conducted in these patients with IFUO (3), Dr Gilutz noted a different follow-up time of 50 months and not 28 months.

He thus questioned whether these observations were due to a typo or corresponded to an interesting and relevant finding.

Here are some key-points to respond:

- There is no typo. In the article on the detailed analysis of IFUO patients (3), the median follow-up time of 50 months regards our entire cohort of 693 GCA patients, and not only IFUO patients. The follow-up time of IFUO patients is unchanged at 28 [0-139] months.
- To determine whether patients with IFUO might have a higher risk of dying earlier after diagnosis, we provide 3 new analyses.
  - In Table I we analysed and compared post-diagnosis times, till death occurred, between the four groups. Although this time was shorter in patients with IFUO, the difference was not statistically significant.
  - In Table II we analysed the cause of death in the 20 patients with IFUO who died. Although some causes might be linked to GCA (*e.g.* stroke), most causes were probably not linked to GCA. Within the IFUO group, the median age of patients who died (78 [57–89] years) was significantly higher than that of those remaining alive (68 [48–85] years, p=0.0001).
  - Finally, we analysed overall survival in the four clinical patterns using life tables and the Kaplan-Meier method, and these were compared using the log-rank test. The statistical analyses were computed using JMP 9.0.1 (SAS Institute Inc., Cary, NC, USA). As shown in Figure 1, survival was not statistically different between the four groups (p=0.10).

To conclude, we thank Dr Gilutz for his careful analysis that allows us to better specify the context and data of our two studies regarding the clinical patterns of GCA. Although some slight differences regarding mortality were observed in the four groups, we did not identify any relevant survival findings. A longer follow-up time may modify these results.

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Table I. Overall survival in the four different disease patterns of giant-cell arteritis.

	Isolated cranial GCA (n=163)	Symptomatic large-vessel GCA (n=18)	GCA as isolated IFUO (n=20)	GCA as clinically clinically isolated PMR (n=1)	*p*
Median survival, months	48 [0-279]	64 [0-264]	30 [0-139]	12	0.64

Table II. Characteristics of patients with inflammation or fever of unknown origin who died.

Patients	Time of death post- diagnosis	Cause of death
Woman, 78 y	Day 6	Stroke
Man, 75 y	Month 1	Stroke
Woman, 86 y	Month 2	Heart failure
Man, 72 y	Month 100	Pulmonary embolism
Man, 78 y	Month 139	Leukaemia
Woman, 76 y	Month 2	Fall + infection
Woman, 72 y	Month 28	Unknown
Man, 82 y	Month 32	Unknown
Woman, 87 y	Month 36	Infection
Woman, 81 y	Month 22	Rupture of cerebral aneurysm
Woman, 88y	Month 5	Infection
Woman, 73 y	Month 138	Heart failure
Man, 82 y	Month 34	Unknown
Woman, 75 y	Month 2	Digestive haemorrhage
Man, 89 y	Month 36	Infection
Man, 77 y	Month 67	Fall + infection + dementia
Man, 85 y	Month 5	Myeloma
Female, 57 y	Month 120	Infection + Mastocytosis
Female, 70 y	Month 23	Stroke
Female, 79 y	Month 61	Heart failure

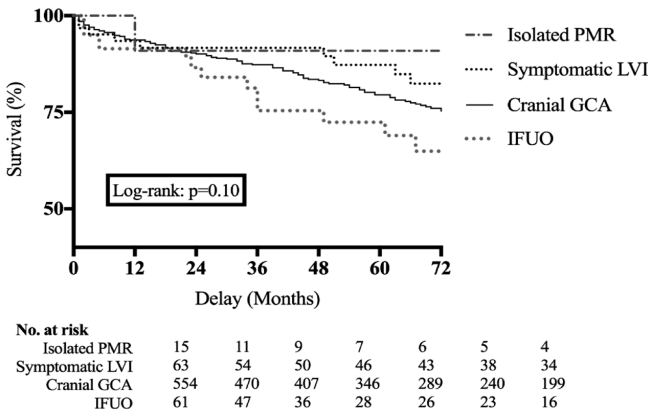

Fig. 1. Kaplan-Meier curves of survival in the four clinical patterns of giant cell arteritis.

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Competing interests: none declared.

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