Intensive versus minimalist follow-up in patients treated for endometrial cancer: A multicentric randomized controlled trial (The TOTEM study—NCT00916708).

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Background: Intensive follow-up in cancer patients, which absorbs a lot of health system resources and can be a source of increased stress for patients, are often proposed on the assumption that an early recognition of relapse will translate in better outcomes. In endometrial cancer few randomized controlled trials were conducted to assess the role of a reduced number of the scheduled visits and of different settings of the follow-up, but did not investigate the contribution of routine serum, cytological or imaging follow-up investigations in improving overall survival or quality of life. The TOTEM study was planned to compare an intensive (INT) vs minimalist (MIN) 5-year follow-up regimen in endometrial cancer patients in terms of overall survival (OS). Methods: Patients surgically treated for endometrial cancer, in complete clinical remission confirmed by imaging, FIGO stage I-IV, were stratified by center and in low (LoR) or high (HiR) risk of recurrence and then randomized to INT or MIN hospital-based follow-up regimens. The main study hypothesis was to demonstrate an improvement from 75% to 80% (expected hazard ratio, HR = 0.78) of the 5-year OS with the INT regimen. Secondary objectives were to compare relapse free survival (RFS), health-related quality of life (HRQL) assessed at baseline, at 6 and 12 months and then yearly (with the SF-12 Physical and Mental Health Summary Scale) and costs. Results: 1884 patients were randomized in 42 centers between 2008 and 2018, and 1847 patients were available for the final analysis (60% LoR). Compliance with the follow-up scheduled visits was 75.3%, similar between INT (74.7%) and MIN (75.9%) arms, whereas the mean number of recorded exams (laboratory or imaging) was markedly higher in the INT than in the MIN arms (9.7 vs 2.9, p < 0.0001). After a median follow-up of 66 months, the overall 5-year OS was 91.3%, 90.6% in the INT and 91.9% in the MIN arms, respectively (HR = 1.12, 95%CI 0.85-1.48, p = 0.429). Comparing the INT vs MIN arms, the 5-year OS were 94.1% and 96.8% (HR = 1.48, 0.92-2.37, p = 0.104) in the LoR and 85.3% and 84.7% (HR = 0.96, 0.68-1.36, p = 0.814) in the HiR group. No relevant differences emerged in RFS between INT and MIN regimens, (HR = 1.13, 0.87-1.48, p = 0.365). At the time of the relapse most women were asymptomatic (146/228, 64.0%), with a tendency of higher proportions in the INT than in the MIN arm, both in the LoR group (78.8% vs 61.1%, p = 0.070) and in the HiR one (64% vs 60%, p = 0.754). HRQL was available only for a subgroup of patients (50% at baseline) and did not differ between arms. Conclusions: Intensive follow-up in endometrial cancer treated patients showed a weak and uncertain advantage in detecting earlier asymptomatic relapses but did not improve OS, even in HiR patients, nor influenced HRQL. Frequent routine use of imaging and laboratory exams in these patients should be discouraged. Clinical trial information: NCT00916708. Research Sponsor: Rete Oncologica Piemonte e Valle d'Aosta.