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Patient Health Protection

European Medicines Agency 2011 Priorities for Drug Safety Research

Epoetins and tumour progression, shortened survival, mortality and thromboembolic events

The results of the Cochrane meta-analysis Erythropoeisis Stimulating Agents (ESA) support previous results concerning a trend in excess mortality and decreased overall survival in ESA-treated patients with malignancies. No answers could be given in this meta-analysis with respect to interactions between ESA treatment and haemoglobin ceilings, ESA dosages and mortality. Further analyses of the individual patient data meta-analysis are planned by the Cochrane study group, i.e. tumour progression and thromboembolic endpoints, and the influence of the actually achieved haemoglobin level on outcomes. These analyses are statistically difficult because of the interaction between the stage of tumour disease and haemoglobin levels.

Also, there is no reassurance on whether the use of ESAs in patients with pre-dialysis renal insufficiency or end stage kidney disease (EKD), including those with concomitant diseases and risk factors like DM2, under the new dosage regimens does not harm these patients.

The uncertainty remains in respect of the appropriateness of the haemoglobin target levels recommended at present and which have been included in 2008 in the SmPCs of ESAs. Therefore large observational studies should be conducted to substantiate the safety of ESA use as currently recommended.

Observational cohort studies should address the remaining concerns of the safety of ESA treatments in patients undergoing chemotherapy and should assess small relative risk differences of mortality or other clinical outcomes. An appropriately considered study design could limit baseline imbalances observed in previous studies by defining patient inclusion criteria, e.g. same haemoglobin levels, tumour stage etc. It is recommended to evaluate whether a sufficient number of patients could be recruited using the restricted inclusion criteria, though one should have in mind that a well designed study would need a long time until results are available.

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