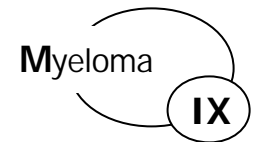




MYELOMA IX TRIAL



PROTOCOL SUMMARY

INDICATION Multiple myeloma requiring treatment (International Myeloma Working Group definition) in patients of all age groups.

OBJECTIVES **For ‘younger/fitter’ patients considered appropriate for high-dose chemotherapy**

Primary

- To compare two induction regimens, CVAD (infusional) v C-Thal-Dex (CTD) (oral)
- To compare two bisphosphonates, namely sodium clodronate (2nd generation) v zoledronic acid (3rd generation)
- To assess the value of giving low-dose thalidomide in maintenance (versus no treatment)
- To assess low-intensity conditioning (LIC) (non-ablative) allogeneic stem cell transplantation (‘mini-allograft’) following standard high-dose melphalan with autograft in patients with donors available.

For ‘older/less fit’ patients considered not appropriate for high-dose chemotherapy

Primary

- To compare two induction/consolidation regimens, MP v C-Thal-Dex attenuated (CTDa)
- To compare two bisphosphonates, namely sodium clodronate (2nd generation) v zoledronic acid (3rd generation)
- To assess the value of giving low-dose thalidomide in maintenance (versus no treatment).

Secondary (all patients)

- To investigate quality of life in the short-term (during induction chemotherapy/bisphosphonate treatment) and in the long-term (during maintenance therapy)
- To determine the relevance of genetic/cytogenetic changes and define risk groups
- To determine the relevance of immunophenotypic changes and molecular evidence of residual disease
- To evaluate serum free light chain (flc) measurement as a prognostic factor and in monitoring disease
- To determine the relevance of biochemical markers of bone metabolism in monitoring disease.

POPULATION

- Patients with multiple myeloma (myelomatosis) of all ages = 18 years
- Written informed consent
- Excluded if prior chemotherapy
- Excluded if more than limited local radiotherapy given
- Excluded if concurrent other active malignancy
- Excluded if pregnant or lactating, or of childbearing potential unwilling to use contraception.

LOCATION 100+ hospitals in the UK, New Zealand and South Africa, involving >300 physicians.

SAMPLE SIZE 1600 patients required over a 5-year recruitment period

STUDY DESIGN There are two main pathways, intensive for 'younger/fitter' patients, non-intensive for 'older/less fit' patients.

Intensive pathway

There are three randomised comparisons within the trial.

- At diagnosis:
 - i) CVAD v CTD
 - ii) Sodium clodronate v Zoledronic acid.
- After high-dose consolidation therapy:
 - iii) Thalidomide v no maintenance therapy.

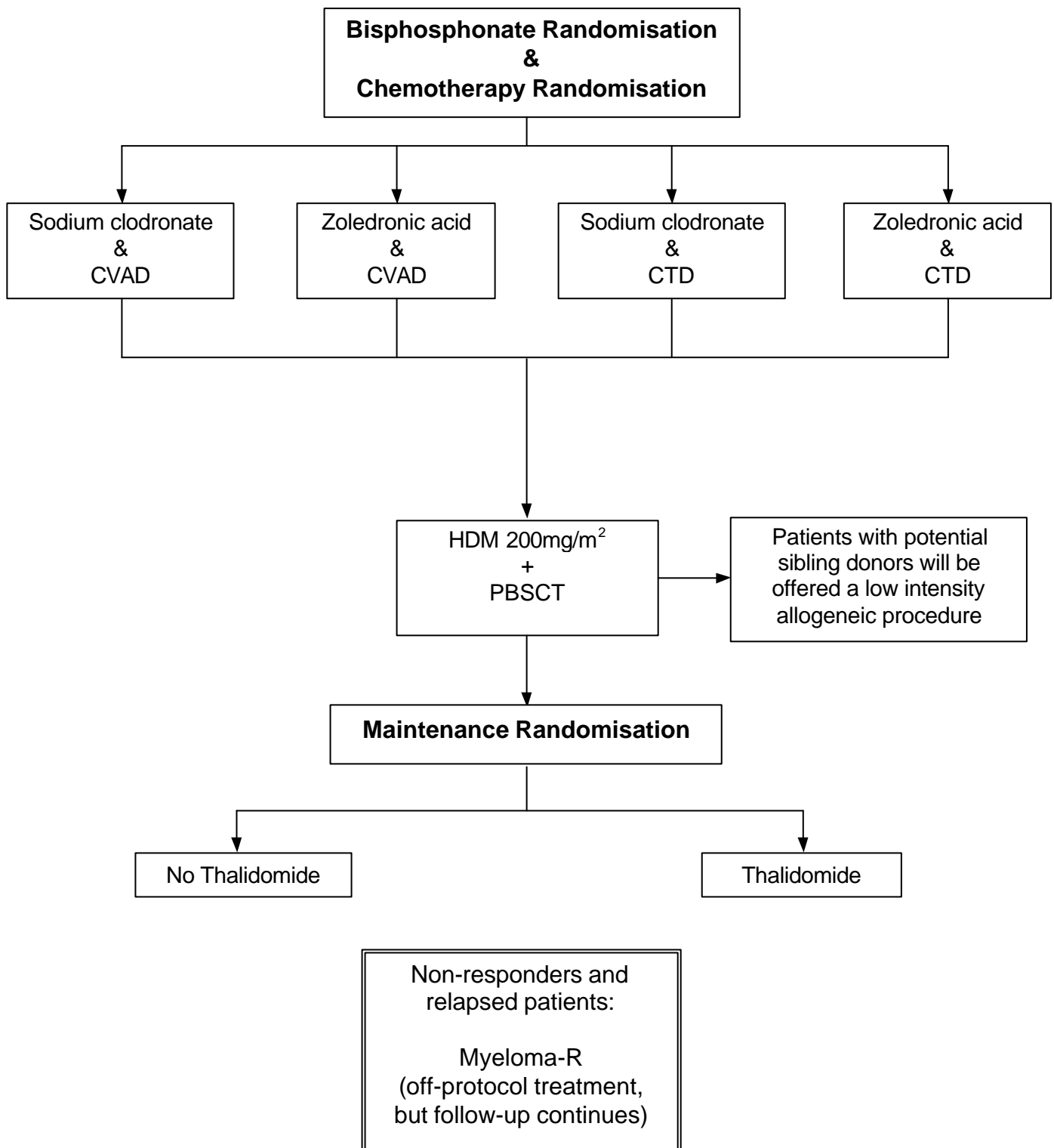
Note: LIC allograft will be offered as additional therapy to patients with sibling donors, but these patients will not be eligible for thalidomide maintenance randomisation.

Non-intensive pathway

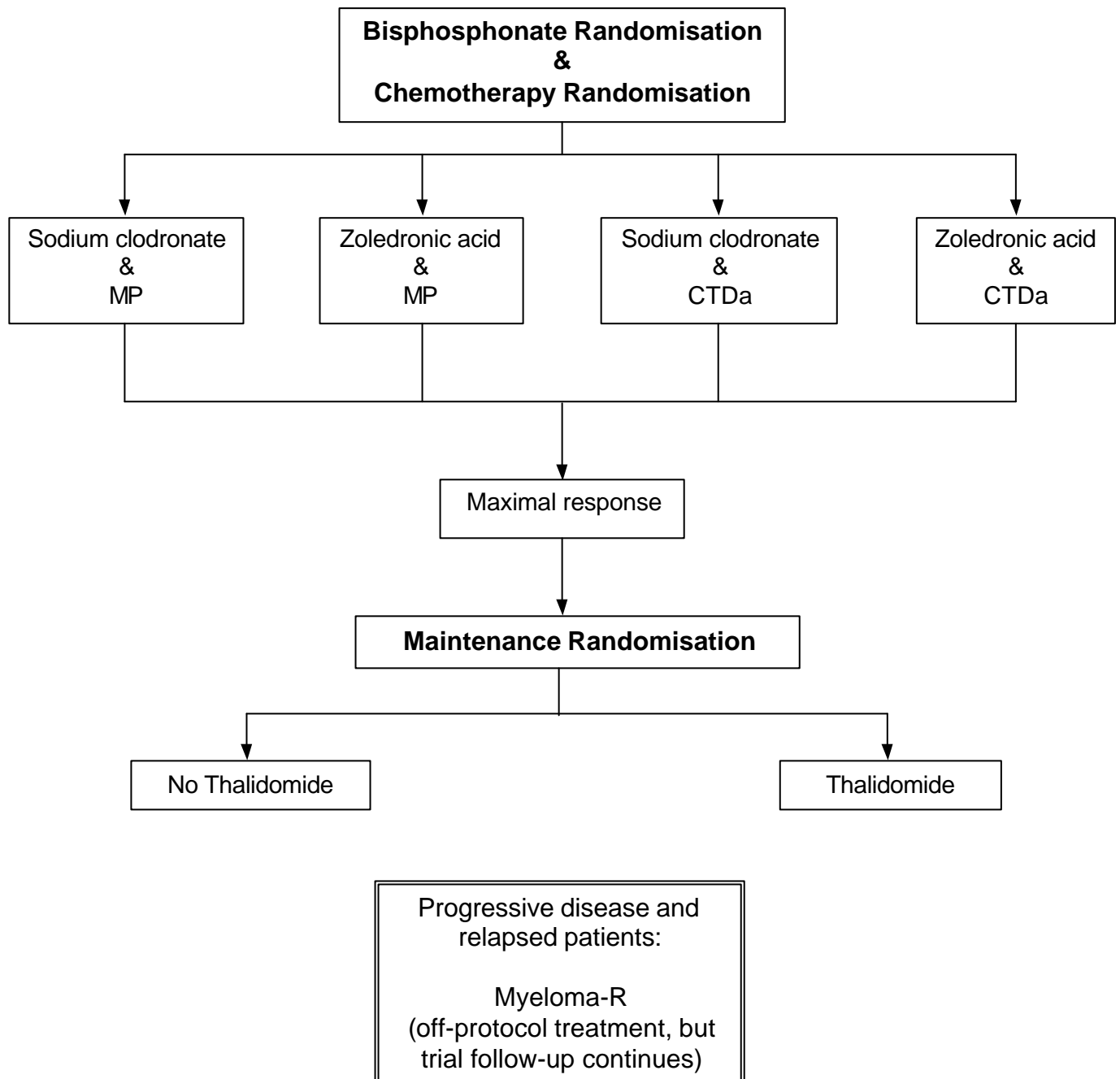
There are three randomised comparisons within the trial.

- At diagnosis:
 - i) MP v CTDa
 - ii) Sodium clodronate v Zoledronic acid.
- After achievement of plateau state:
 - iii) Thalidomide v no maintenance therapy.

Intensive pathway outline



Non-intensive pathway outline



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