Immunoparesis status in immunoglobulin light chain amyloidosis at diagnosis affects response and survival by regimen type

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Supplementary

Calculation of average relative difference (ARD) of the uninvolved immunoglobulins

The uninvolved immunoglobulins are identified by omitting any intact immunoglobulin shown on immunofixation, and for which its light chain component was proven to be the amyloidogenic source.

Then, the relative difference (RD) of each uninvolved immunoglobulin is calculated as follows:

$$\frac{\text{(Level of the uninvolved immunoglobulin at diagnosis)} - \text{(Corresponding LLN)}}{\text{Corresponding LLN}}$$

LLN represents the lower limit of normal. The LLN in the local laboratory reference and are:

For IgG: 767 mg/dL

For IgA: 61 mg/dL

For IgM: 37 mg/dL

Then, the average value of all RDs is calculated to create the average relative difference (ARD) of the uninvolved immunoglobulins.

Sample calculation of ARD:

Patient with lambda light chain amyloidosis with cardiac and autonomic/peripheral nervous system involvement. Levels of the uninvolved immunoglobulins at presentation were: IgG 558 mg/dL, IgA 74 mg/dL, IgM 24mg/dL

The RD of each uninvolved immunoglobulin was calculated as follows:

RD of uninvolved IgG: (558-767)/767=(-0.27)

RD of uninvolved IgA: (74-61)/61=0.21

RD of uninvolved IgM= (24-37)/37=-0.35

And the ARD is calculated as follows: [(-0.27) + 0.21 + (-0.35)]/3=-0.13 or -13%

Type of regimens used at first line of treatment:

- **Autologous stem cell transplantation (ASCT) (n=289):**
    - Upfront ASCT (n=220)
    - Bortezomib-cyclophosphamide-dexamethasone (n=30)
    - Dexamethasone alone (n=11)
    - Melphalan-dexamethasone (n=9)
    - Bortezomib-dexamethasone (n=9)
    - Lenalidomide-dexamethasone (n=4)
    - Thalidomide-dexamethasone (n=2)
    - Bortezomib alone (n=2)
    - Lenalidomide-cyclophosphamide-dexamethasone (n=2)

- **Melphalan-based regimens (n=220):**
    - Melphalan-dexamethasone (n=213)
    - Melphalan-prednisone (n=7)

- **Bortezomib-based regimens (n=131):**
    - Bortezomib-cyclophosphamide-dexamethasone (n=97)
    - Bortezomib-dexamethasone (n=18)
    - Bortezomib-melphalan-dexamethasone (n=13)
    - Bortezomib alone (n=3)

- **IMiD-based regimens (n=31):**
    - Lenalidomide-cyclophosphamide-dexamethasone (n=12)
    - Lenalidomide-dexamethasone (n=8)
    - Lenalidomide alone (n=4)
    - Thalidomide-dexamethasone (n=2)
    - Revlimid-bortezomib-dexamethasone (n=2)
    - Thalidomide-melphalan-dexamethasone (n=1)
    - Thalidomide-cyclophosphamide-dexamethasone (n=1)
    - Lenalidomide-melphalan-prednisone (n=1)

- **Dexamethasone alone (n=10)**

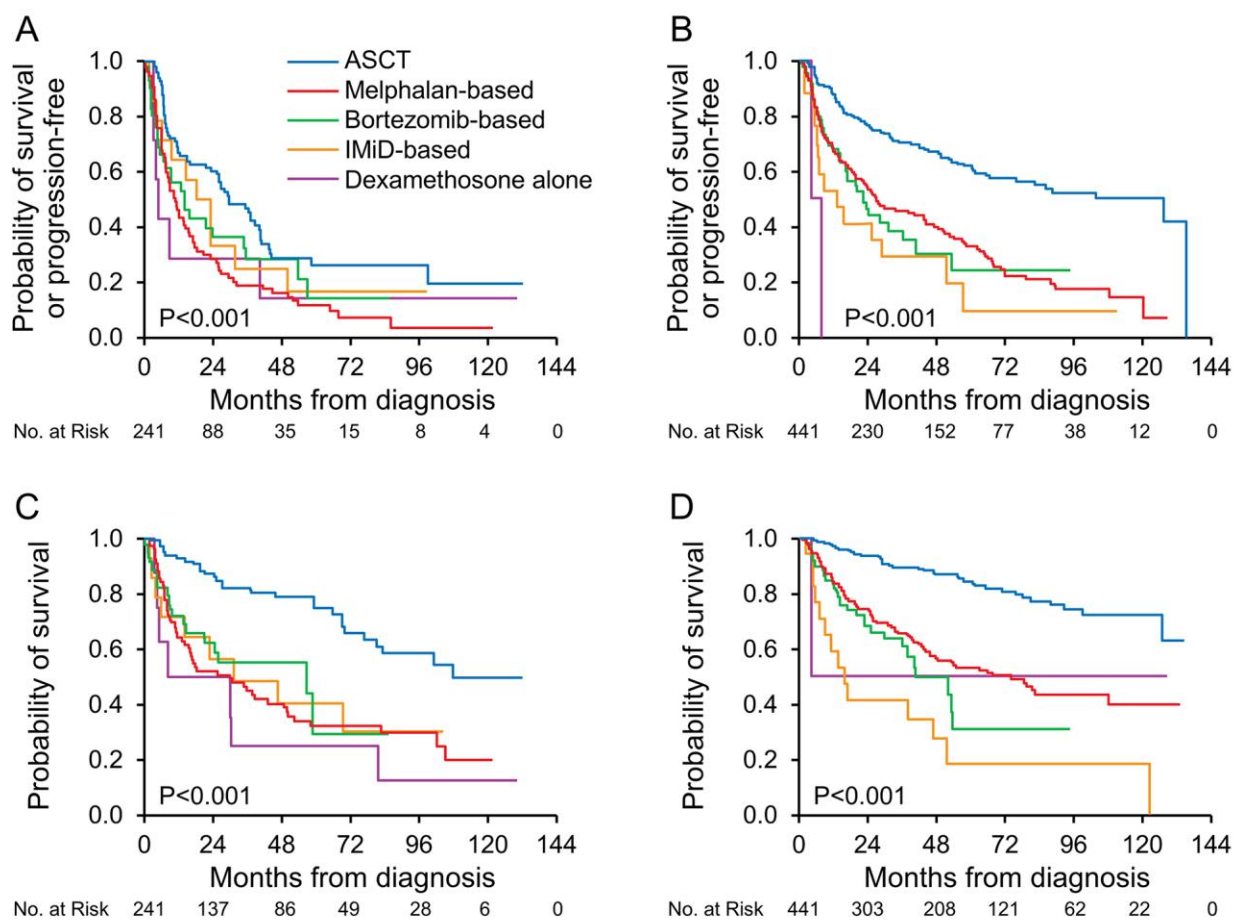**Type of regimens used at first progression:**

- **ASCT (n=12):**
  - ASCT without prior treatment at relapse (n=12)

- **Melphalan-based regimens (n=33):**
  - Melphalan-dexamethasone (n=31)
  - Melphalan-prednisone (n=2)

- **Bortezomib-based regimens (n=127):**
  - Bortezomib-dexamethasone (n=58)
  - Bortezomib-cyclophosphamide-dexamethasone (n=55)
  - Bortezomib alone (n=8)
  - Bortezomib-melphalan-dexamethasone (n=2)
  - Ixazomib-dexamethasone (n=2)
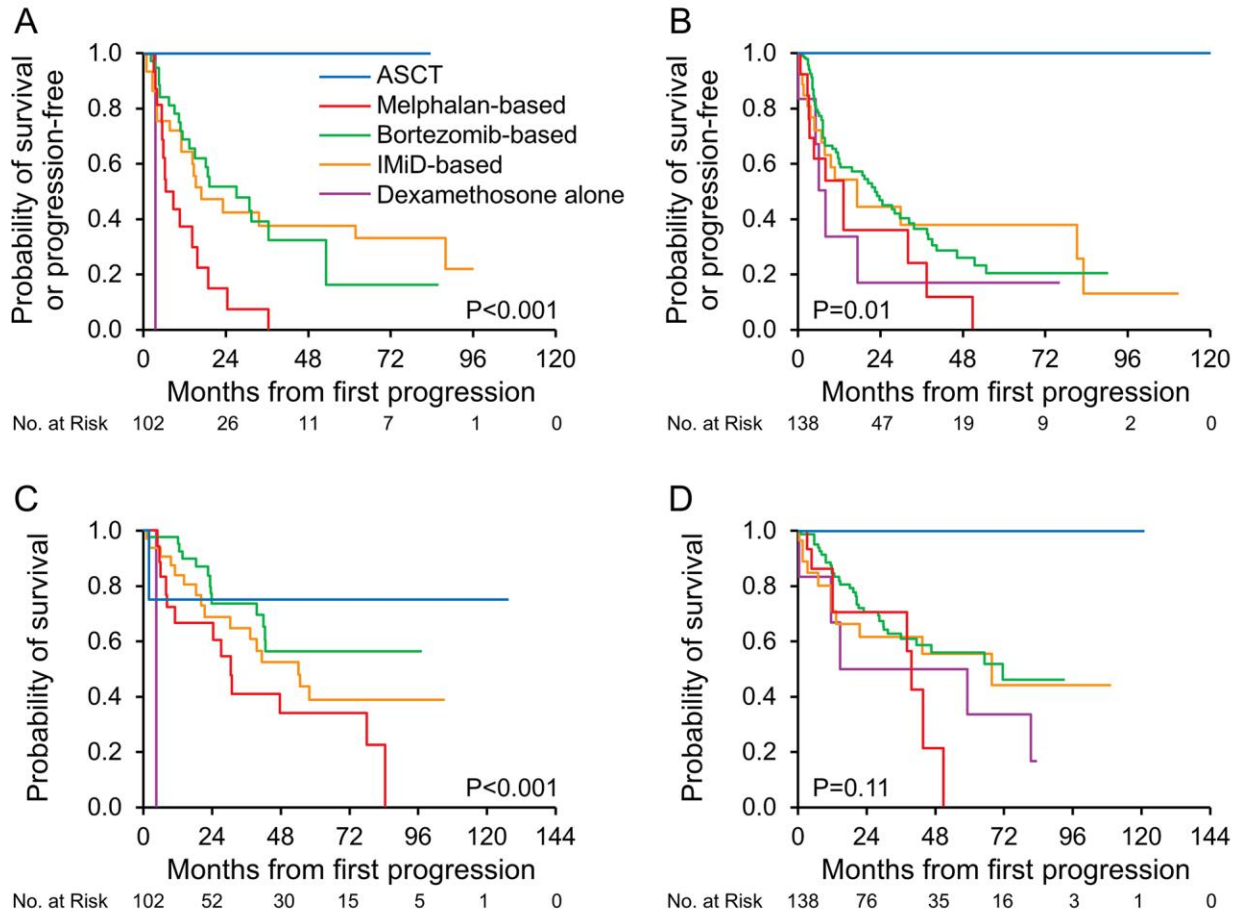 - Carfilzomib-cyclophosphamide-dexamethasone (n=2)

- **IMiD-based regimens (n=61):**
  - Lenalidomide-dexamethasone (n=38)
  - Revlimid-bortezomib-dexamethasone (n=8)
  - Lenalidomide-cyclophosphamide-dexamethasone (n=6)
  - Pomalidomide-dexamethasone (n=5)
  - Thalidomide-dexamethasone (n=3)
  - Lenalidomide alone (n=1)

- **Dexamethasone alone (n=7)**

Supplementary Figure 1: Survival curves at first line treatment by regimen type in each ARD group

- **A.** Progression-free survival in the negative ARD group
- **B.** Progression-free survival in the positive ARD group
- **C.** Overall survival in the negative ARD group
- **D.** Overall survival in the positive ARD group

Supplementary Figure 2: Survival curves at first progression by regimen type in each ARD group

- **A.** Progression-free survival in the negative ARD group
- **B.** Progression-free survival in the positive ARD group
- **C.** Overall survival in the negative ARD group
- **D.** Overall survival in the positive ARD group