**Supplemental Table 1.** ***Results of some recent trials of chemotherapy in MPM*.**

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Patient status** | **Reference** | **Type** | **% Epi** | **# Pts** | **Response rate (%)** | **TTP/PFS**  **(mo)** | **Median OS (mo)** | **1 Yr OS (%)** | **DCR** |
| **Naïve** | Vogelzang [1] | pem/cis | 68 | 168 | 46 | 6.1 | 13.3 | 57 |  |
| Van Meerbeeck [2] | ralitrexed/cis | 75 | 126 | 24 | 5.3 | 11.4 | 46 |  |
| Lee [3] | carbo/pem |  | 37 | NR | NR | 10 | 41 |  |
| Ceresoli [4] | carbo/pem | 78 | 102 | 19 | 6.5 | 12.7 | 51 |  |
|  | Krug [5] | Pem/Cis |  | 30 | 10 | 3.4 | 12.8 | 50 (est) | 60 |
|  | Santoro [6] | pem/cis (Int. expanded access trial) | 67 | 745 | 26 | 7 | not avail | 63 | 78 |
|  |  | pem/carbo (Int. expanded access trial) | 67 | 752 | 22 | 6.9 | not avail | 64 | 76 |
|  |  |  |  |  |  |  |  |  |  |
|  | **Average** |  | **71** |  | **25** | **5.9** | **12** | **53** | **71** |
|  | Hassan [7] | Meso Ab and pem cis | 89 | 89 | 40 | 6.1 | 14.8 | 60 | 91 |
|  |  |  |  |  |  |  |  |  |  |
| **Naive** | **current trial** |  | **61** | **18** | **28** | **6.5** | **12** | **55** | **83** |
|  |  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |
| **Pre-treated** | Zucali [8] | prior pem, then  gem or vinorelbine |  | 30 | 10 | 2.8 | 10.9 | NR |  |
| Xanthopoulos [9] | prior pem, then -oxali/gem |  | 29 | 22 | 2.0 | 6.0 | NR |  |
| Stebbing [10] | vinorelbine | 62 | 63 | 16 |  | 9.6 | NR |  |
| Pasello [11] | carbo/gem |  | 17 | NR | 3.6 | 6.6 | NR |  |
| Dubey [12] | sorafenib |  | 50 | NR | 3.6 | 9.7 | NR |  |
| Margery [13] | pem or gem/oxali |  | 44 | NR | 3.8 | 12.2 | NR |  |
| Ceresoli [14] | re-treat with pem |  | 31 | 19 | 3.8 | 10.5 | NR |  |
|  | Zucali (15) | prior pem/cis retreat with vinorelbine | 90 | 59 | 15 | 2.3 | 6.2 | 25 (est) | 52 |
|  | Zucali [16] | review 2L (all) | 75 | 181 | 11 | 4.3 | 8.7 | 34 | 71 |
|  |  |  |  |  |  |  |  |  |  |
|  | Zucali [16] | Pem retreated with Pem |  | 42 | ? | 6.5 | 11 | 50 | 65 |
| **Patient status** | **Reference** | **Type** | **% Epi** | **# Pts** | **Response rate (%)** | **TTP/PFS**  **(mo)** | **Median OS (mo)** | **1 Yr OS (%)** | **DCR** |
|  | Zauder [17] | Pem/cis retreated with Gem or Venorelbine | 67 | 60 | 2 | 1.7 | 5.2 | NR | 48 |
|  | Nowack [18] | Pem/cis treated with BNC105 | 67 | 30 | 3 | 1.5 | 8.2 | 45 (est) | 46 |
|  | Calabro [19] | Pem/cis treated with tremilumimab | 86 | 29 | 7 | 6.2 | 10.7 | 48 | 31 |
|  | **Average** |  |  |  | **11** | **3.5** | **9.0** | **44** | **52** |
|  | **Current Trial** | **All 2nd line** |  | **22** | **14** | **4.0** | **17** | **60** | **91** |
|  |  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |
|  | Zucali [16] | review 2L (all) | 75 | 181 | 11 | 4.3 | 8.7 | 34 | 71 |
|  | **Current Trial** | **All 2nd line** |  | **22** | **14** | **4.0** | **17** | **60** | **91** |
|  |  |  |  |  |  |  |  |  |  |
| **Pem retreated with PEM** | Zucali [16] | Pem retreated with Pem |  | 42 | ? | 6.5 | 11 | 50 | 65 |
|  | Ceresoli [14] | Pe,m re-treat with pem |  | 31 | 19 | 3.8 | 10.5 | NR |  |
|  | Bearz | Pem, re-treat with pem |  | 30 | 17 | 5.1 | 13.6 | 50  (2 yr-30%) | 67 |
|  | Average |  |  |  | **18** | **5.1** | **11.7** | **50** | **66** |
|  | **Current Trial** | **Prior Pem- repeat Pem** |  | **7** | **28** | **8.0** | **26** | **86** | **86** |
|  |  |  |  |  |  |  |  |  |  |
| **Patient status** | **Reference** | **Type** |  | **# Pts** | **Response rate (%)** | **TTP/PFS**  **(mo)** | **Median OS (mo)** | **1 Yr OS (%)** | **DCR** |
|  |  |  |  |  |  |  |  |  |  |
| **All patients** | Current Trial |  |  | 40 | 25 | 5.3 | 13 | 60 | 88 |
| **Naïve** | Current Trial | Pem/cis |  | 18 | 28 | 6.5 | 12 | 55 | 83 |
| **Pre-treated** | Current Trial | All 2nd line |  | 22 | 14 | 4.0 | 17 | 60 | 91 |
|  |  | Prior Pem- repeat Pem |  | 7 | 28 | 8.0 | 26 | 86 | 100 |
|  |  | Prior Pem repeat GEM |  | 15 | 7 | 3.5 | 10 | 47 | 87 |

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Supplemental Table 2. Post-Trial Therapies

|  |  |  |
| --- | --- | --- |
| **ID** | **Post Dosing Treatment** | **1st Line or 2nd Line** |
| 402 | Navelbine x 1 course | 2 |
| 404 | TGF-beta, CIR T cells, Pem X 1 cycle | 2 |
| 405 | Liver immunoembolization @ TJUH | 2 |
| 406 | Gem maintenance | 1 |
| 407 | Radiation | 2 |
| 408 | 06511-GEM +/- NGR-hTNF X2 | 1 |
| 409 | None | 2 |
| 410 | None | 1 |
| 411 | CIR T cells, PEMX 3, Rad, Consented for AdV-tk trial Dose #2(#2 patient), palliative RT cervical nodale mass | 2 |
| 412 | None | 1 |
| 413 | None | 1 |
| 416 | Rad, SBRT 2/13, Pem(3/13-10/13) | 2 |
| 417 | Gem maintenance 5/12-6/14, Cytoreductive surgery, tremelimumab study | 2 |
| 418 | Maintenance PEM/Gem 10/13-8/14, Pem 9/14 | 2 |
| 419 | Palliative Rad for pain | 1 |
| 420 | Recent progression-treatment with PEM. | 2 |
| 421 | None | 2 |
| 422 | None | 2 |
| 423 | Palliative RT | 1 |
| 424 | Palliative RT-CTCA/Home Hospice | 1 |
| 425 | Maintenance PEM/PD on 2/1013 CT GEM started | 2 |
| 426 | Home Hospice | 1 |
| 427 | UPCC 06511/gem +/- NGR-hTNFX2 treatments | 1 |
| 428 | Rad to pleural cath site. Hospice | 1 |
| 429 | PEM maintenance | 1 |
| 430 | Gem maintenance; AdV-tk(L2), palliative radiation with hyperthermia | 2 |
| 431 | Pem maintenance;AdV-tk trial Dose Level #2 on 12/2/13(#1)-GEM, Palliative RT, Navelbine | 1 |
| 432 | PEM maintenance | 1 |
| 433 | PEM/carbo, palliative radiation, Pem/carboX3 C, PEM, GEM locally, Considering T cell | 2 |
| 434 | None | 2 |
| 435 | Navelbine locally-started 4/13 | 2 |
| 436 | Pleurectomy/PDT-5/20/14/Carbo-Alimta X6 cycles, ?proton tx | 1 |
| 437 | C30901-Randomized to Pem maintenance(versus observation) | 1 |
| 438 | Pem maintenance, Gem, Tremelilumimab vs. Placebo, Navelbine | 2 |
| 439 | Rad to pleural cath site/Pem maintenance | 1 |
| 441 | Pem maintenance/Proton Tx to pleurx site; T cell meso trial, Lilly trial LY3023414 | 2 |
| 442 | Tremelimumab study-Duke(1/14-4/14)Navelbine locally | 2 |
| 443 | None | 1 |
| 445 | Palliative Rad txp | 2 |
| 446 | Tremimulimab trial at Duke | 2 |
|  |  |  |

**Supplemental Table 3. Characteristics of Patients Selected for Flow Cytometry Analysis**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Pt Number | Line of Rx | survival (11/2013) | ave survival | selection code | RECIST Response | ave response | Antibody Response | type of chemo |
| 404 | 2 | 15 |  | responder | -7% |  | 0 | G |
| 411 | 2 | 33 |  | responder | -6% |  | 0 | G |
| 416 | 2 | 25 |  | responder | -12% |  | 0 | G |
| 406 | 1 | 21 |  | responder | -48% |  | 1 | P |
| 405 | 1 | 40 |  | responder | -32% |  | 2 | P |
| 417 | 2 | 31+ |  | responder | 13% |  | 2 | G |
|  |  |  | 26.8 mo |  |  | -15.3% |  |  |
| 425 | 2 | 9 |  | non-responder | -19% |  | 1 | P2 |
| 402 | 2 | 6.5 |  | non-responder | 10% |  | 2 | G |
| 421 | 2 | 5 |  | non-responder | 5% |  | 2 | G |
| 422 | 2 | 2.5 |  | non responder | 80% |  | 2 | P2 |
| 429 | 1 | 9 |  | non responder | -14% |  | 1 | P1 |
| 423 | 1 | 11 |  | non responder | -4% |  | 1 | P1 |
|  |  |  | 7.2 mo |  |  | 9.7% |  |  |
| Antibody Code: 0= no change, 1= marginal changes, 2= significant changes | | | | | |  |  |  | |  |

|  |
| --- |
| **CCL5** |
| **CD3D** |
| **CD86** |
| **CD8a** |
| **CDC42SE1** |
| **CXCL10** |
| **CXCL2** |
| **CXCL9** |
| **EPSTI1** |
| **GBP1** |
| **GCH1** |
| **GZMK** |
| **ICOS** |
| **IL2RG** |
| **IRF1** |
| **ITK** |
| **KLRD1** |
| **PSMB8** |
| **PSMB9** |
| **PTGER4** |
| **SLAMF6** |
| **SLAMF7** |
| **STAT1** |
| **TARP** |
| **TNFAIP3** |
| **TNFRSF9** |
| **TOX** |

**Supplemental Table 4. List of Immune Response Genes assayed by Nanostring**

**Supplemental Table 5: Correlation of Antibody Response to MOS or Radiographic Response**

|  |  |  |  |
| --- | --- | --- | --- |
| Antibody Response | N | MOS (months) | Response (% change) |
| 0 | 11 | 13.0 | 0% |
| 1 | 14 | 14.0 | -12% |
| 2 | 14 | 12.5 | 7% |
| p value |  | NS | NS |

**Supplemental Table 6. Flow Cytometry Results**

|  |  |  |  |
| --- | --- | --- | --- |
|  | CD8 T cells: % positive for CD69 | | |
|  | Baseline | D2 | D15 |
| Good responders | 17.0  (IQR 15.5-23.4) | 26.6  (IQR: 23.2-44.9) | 16.6  (IQR: 11.5-22.4) |
| Poor  Responders | 11.4  (IQR: 9.3-20.9) | 22.1  (IQR: 9.9-36.6) | 14.9  (IQR: 10.5-44.8 |
| p value: good vs bad responders | 0.235 | 0.235 | 1 |
|  |  |  |  |
|  |  |  |  |

|  |  |  |  |
| --- | --- | --- | --- |
|  | NK Cells: % positive for CD69 | | |
|  | Baseline | D2 | D15 |
| Good responders | 21.7  (IQR: 8.3-22.7) | 66.6\*  (IQR: 42.1-79.0) | 20.9  (IQR: 5.8-31.4) |
| Poor Responders | 17.5  (IQR: 11.1-24.6) | 33.3  (IQR: 22.8-73.0) | 22.7  (IQR: 13.2-44.6) |
| p value g vs b | 1 | .298 | 0.92 |
|  |  |  |  |
| \*P=0.03 vs baseline |  |  |  |