

Supplementary table 1a

| Patient baseline characteristics, Cohort A (n=30) | | | | | |
|---|---------------------|---------|--------------|-------------|------------------------|
| Patient ID | Previous treatment | M-stage | PD-L1 status | BRAF status | LDH elevation (yes/no) |
| MM1636.01 | None | M1c | <1% | Wildtype | Yes |
| MM1636.02 | None | M1a | <1% | Mutated | Yes |
| MM1636.03 | None | M1c | >1% | Mutated | Yes |
| MM1636.04 | 1. line ipilimumab | M1b | <1% | Wildtype | No |
| MM1636.05 | None | M1c | >1% | Wildtype | Yes |
| MM1636.06 | Adjuvant ipilimumab | M1a | >1% | Mutated | No |
| MM1636.07 | None | M1a | >1% | Wildtype | No |
| MM1636.08 | 1. line ipilimumab | M1c | <1% | Wildtype | Yes |
| MM1636.09 | None | M1c | <1% | Wildtype | No |
| MM1636.10 | None | M1c | >1% | Mutated | No |
| MM1636.11 | None | M1a | <1% | Mutated | No |
| MM1636.12 | None | M1a | >1% | Mutated | No |
| MM1636.13 | None | M1c | >1% | Wildtype | Yes |
| MM1636.14 | None | M1c | <1% | Mutated | No |
| MM1636.15 | None | M1c | <1% | Wildtype | Yes |
| MM1636.16 | None | M1c | > 1% | Mutated | No |
| MM1636.17 | None | M1b | > 1% | Wildtype | No |
| MM1636.18 | None | M1b | < 1% | Wildtype | No |
| MM1636.20 | None | M1c | < 1% | Mutated | No |
| MM1636.22 | None | M1b | >1% | Wildtype | No |
| MM1636.23 | None | M1c | <1% | Wildtype | No |
| MM1636.24 | None | M1c | >1% | Wildtype | No |
| MM1636.27 | None | M1c | >1% | Mutated | No |
| MM1636.29 | None | M1b | > 1% | Wildtype | No |
| MM1636.34 | None | M1c | < 1% | Wildtype | Yes |
| MM1636.35 | None | M1c | > 1% | Wildtype | Yes |
| MM1636.37 | None | M1a | <1% | Mutated | No |
| MM1636.38 | None | M1a | >1% | Wildtype | Yes |
| MM1636.39 | None | M1b | >1% | Wildtype | No |
| MM1636.42 | None | M1c | >1% | Wildtype | Yes |

Supplementary table 1b

| Sub-group information, Cohort A (n=30) | | | | | | |
|--|-----------------|---------------|---------------------|---------------------|-------------------------------|---------------------------|
| Characteristic - no. | M1a+b (n=13) | M1c (n=17) | PD-L1 >1% (n=17) | PD-L1 <1% (n=13) | LDH non-elevated (n=19) | LDH elevated (n=11) |
| Previous treatment | | | | | | |
| None | 11 | 16 | 16 | 11 | 17 | 10 |
| 1. line ipilimumab | 1 | 1 | 0 | 2 | 1 | 1 |
| Adjuvant ipilimumab | 1 | 0 | 1 | 0 | 1 | 0 |
| BRAF status | | | | | | |
| Mutated | 5 | 6 | 6 | 5 | 9 | 2 |
| Wildtype | 8 | 11 | 11 | 8 | 10 | 9 |
| LDH status | | | | | | |
| Elevated | 2 | 9 | 6 | 5 | | |
| Non-elevated | 11 | 8 | 11 | 8 | | |
| PD-L1 status | | | | | | |
| <1% | 5 | 8 | | | 8 | 5 |
| >1% | 8 | 9 | | | 11 | 6 |
| M stage | | | | | | |
| M1a+b | | | 8 | 5 | 8 | 2 |
| M1c | | | 9 | 8 | 11 | 9 |

Supplementary table 2

| Detailed treatment information, Cohort A (n=30) | | | | | | |
|---|-----|-----------------|----------------------------------|-----------------------------------|-----------------------------------|-----------------------------------|
| Patient ID | BOR | vaccines series | Number nivolumab series (3mg/kg) | Number nivolumab series (6 mg/kg) | Reason to stop treatment | Subsequent treatment |
| MM1636.01 | CR | 15 | 24 | 5 | Grade 3 rash | |
| MM1636.02 | PD | 5 | 5 | | Progression | Dabrafenib/Trametinib |
| MM1636.03 | CR | 15 | 24 | 9 | Maximum benefit | None |
| MM1636.04 | PD | 5 | 5 | | Progression | Radiotherapy, Temodal |
| MM1636.05 | CR | 13 | 21 | | Grade 2 pneumonitis | None |
| MM1636.06 | CR | 15 | 24 | 9 | Progression | Dabrafenib/Trametinib |
| MM1636.07 | CR | 8 | 12 | 2 | Grade 2 pneumonitis | Reinduction Nivolumab |
| MM1636.08 | PR | 11 | 16 | | Progression | Ipilimumab, Radiotherapy |
| MM1636.09 | PD | 5 | 5 | | Progression | None |
| MM1636.10 | PR | 15 | 24 | 7 | Progression | Encorafenib/Binimetinib |
| MM1636.11 | PD | 3 | 3 | | Progression | Dabrafenib/Trametinib, Ipilimumab |
| MM1636.12 | CR | 15 | 24 | 8 | Maximum benefit | None |
| MM1636.13 | PR | 15 | 24 | 13 | Reached 2 years of treatment | None |
| MM1636.14 | CR | 11 | 16 | | Grade 2 colitis | None |
| MM1636.15 | PR | 15 | 24 | 11 | Reached 2 years of treatment | None |
| MM1636.16 | PR | 9 | 12 | | Progression | T cell therapy CT ID: NCT02278887 |
| MM1636.17 | PD | 6 | 6 | | Progression | None |
| MM1636.18 | CR | 5 | 5 | | Grade 5 toxicity due to nivolumab | None |
| MM1636.20 | CR | 11 | 18 | 2 | Maximum benefit | None |
| MM1636.22 | CR | 15 | 24 | 1 | Grade 3 arthralgia | None |
| MM1636.23 | CR | 15 | 24 | 3 | Maximum benefit | None |
| MM1636.24 | CR | 15 | 24 | | Maximum benefit | None |
| MM1636.27 | CR | 15 | 24 | 3 | Maximum benefit | Encorafenib/Binimetinib |
| MM1636.29 | PR | 15 | 24 | 4 | Apoplexia and Grade 3 hepatitis | Pembrolizumab |
| MM1636.34 | PD | 3 | 3 | | Progression | None |
| MM1636.35 | PR | 15 | 24 | 10 | Reached 2 years of treatment | None |
| MM1636.37 | PR | 7 | 8 | | Progression | Encorafenib/Binimetinib |
| MM1636.38 | CR | 14 | 23 | | Maximum benefit | |
| MM1636.39 | CR | 13 | 19 | | Grade 2 dermatitis | |
| MM1636.42 | PR | 15 | 24 | 9 | Reached 1,5 years of treatment | |

Supplementary table 3

| Immune-related adverse events, Cohort A (n=30) | | | | |
|--|-----------|-----|-----------|----|
| | Grade 1-2 | % | Grade 3-4 | % |
| Vaccine related | | | | |
| Granuloma (injection site) | 20 | 67% | | |
| Injection site reactions | 23 | 77% | | |
| Redness (injection site) | 7 | 23% | | |
| Pruritus (injection site) | 4 | 13% | | |
| Pain (injection site) | 4 | 13% | | |
| Myalgia (injection site) | 1 | 3% | | |
| Respiratory | | | | |
| Pneumonitis | 4 | 13% | | |
| Pleural effusion | 1 | 3% | | |
| Dyspnoea | 7 | 23% | | |
| Gastrointestinal | | | | |
| Diarrhoea | 9 | 30% | 1 | 3% |
| Constipation | 2 | 7% | | |
| Abdominal pain | 4 | 13% | | |
| Colitis | 2 | 7% | 1 | 3% |
| Musculoskeletal | | | | |
| Arthralgia | 9 | 30% | 2 | 7% |
| Myalgia | 5 | 17% | | |
| Endocrinal | | | | |
| Adrenal insufficiency | 2 | 7% | 1 | 3% |
| Hypophysitis | 2 | 7% | | |
| Hypothyroidism | 1 | 3% | | |
| Hyperthyroidism | 2 | 7% | | |
| Skin | | | | |
| Dry skin | 8 | 27% | | |
| Rash | 14 | 47% | 2 | 7% |
| Vitiligo | 4 | 13% | | |
| Pruritus | 8 | 27% | | |
| Vasculitis | 1 | 3% | | |
| Laboratory tests | | | | |
| Increase ALAT | 4 | 13% | | |
| Increased amylase | 6 | 20% | | |
| Hyponatremia | | | 1 | 3% |
| Other | | | | |
| Infusion reaction | 5 | 17% | | |
| Fatigue | 17 | 47% | | |
| Xerostomia | 5 | 17% | | |
| Nausea | 8 | 27% | | |
| Stomatitis | 2 | 7% | | |
| Periorbital oedema | 1 | 3% | | |
| Nasal congestion | 2 | 7% | | |
| Peripheral neuropathy | 1 | 3% | | |
| Dry eyes | 1 | 3% | | |
| Hearing impaired | 1 | 3% | | |

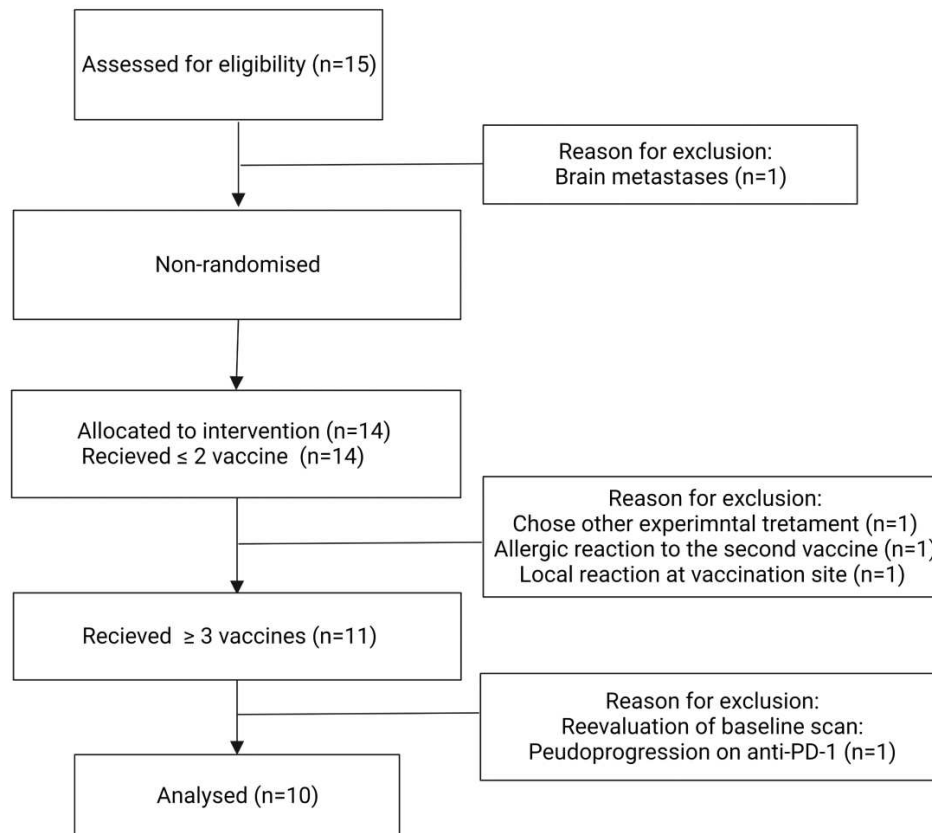
Supplementary table 4

| Detailed patient baseline characteristics, Cohort B (n=10) | | | | | |
|--|---------|--|-----------|-------------|--------------|
| Patient ID | M-stage | Metastatic sites at baseline | LDH (U/L) | BRAF status | PD-L1 status |
| MM1636.21 | M1b | lungs, pleura | 202 | Wild-type | < 1% |
| MM1636.26 | M1a | subcutis, intramuscular, cutis, toe | 187 | Wild-type | < 1% |
| MM1636.30 | M1c | lungs, lymph nodes, subcutis, pancreas, spleen, liver, kidney, peritoneum, bones | 324 | Wild-type | ? |
| MM1636.31 | M1b | lungs | 156 | Wild-type | < 1% |
| MM1636.32 | M1a | subcutis, cutis | 159 | Wild-type | < 1% |
| MM1636.33 | M1c | adrenal glands, lungs | 216 | Wild-type | > 1% |
| MM1636.41 | M1b | lung, muscle, subcutis | 162 | Wild-type | ? |
| MM1636.47 | M1a | lymph nodes | 169 | Wild-type | > 1% |
| MM1636.48 | M1a | subcutis, lymph nodes | 160 | Wild-type | < 1% |
| MM1636.49 | M1b | lungs | 167 | Wild-type | > 1% |

Supplementary table 5

| Treatment details, Cohort B (n=10) | | | | | | | |
|------------------------------------|-----|---------------------------|---------------------------|----------|---------------------------------|---|---|
| Patient ID | BOR | Nivolumab cycles (3mg/kg) | Nivolumab cycles (6mg/kg) | Vaccines | Rational for stopping treatment | Prior treatment | Subsequent treatment |
| MM1636.21 | PD | 6 | | 6 | PD | Pembrolizumab (7 cycles) | Ipilimumab |
| MM1636.26 | PD | 6 | | 6 | PD | Nivolumab (5 cycles) | Ipilimumab |
| MM1636.30 | PD | 4 | | 4 | PD | Ipilimumab (4 cycles), Pembrolizumab (16 cycles), IL-2 (4 cycles) Temozolomide (6 cycles) | None |
| MM1636.31 | PD | 6 | | 6 | PD | Pembrolizumab (16 cycles) | Ipilimumab, Phase I Robust trial, BP41628, PD1-IL2v. Temozolomide |
| MM1636.32 | PD | 6 | | 6 | PD | Nivolumab (5 cycles) | Ipilimumab |
| MM1636.33 | SD | 10 | 1 | 9 | PD | Pembrolizumab (4 cycles) Ipilimumab (3 cycles) | Temozolomide |
| MM1636.41 | PD | 6 | | 6 | PD | Nivolumab (7 cycles) | Ipilimumab |
| MM1636.47 | SD | 12 | | 9 | PD | Pembrolizumab (7 cycles) | Ipilimumab |
| MM1636.48 | PD | 4 | | 4 | PD | Pembrolizumab (9 cycles) | None |
| MM1636.49 | PD | 5 | | 5 | Treatment ongoing | Pembrolizumab (6 cycles) | Ipilimumab |

Supplementary table 6



Supplementary table 7

| Immune-related adverse events, Cohort B (n=10) | | | | |
|--|-----------|-----|-----------|-----|
| | Grade 1-2 | % | Grade 3-4 | % |
| Vaccine-related | | | | |
| Granuloma (injection site) | 4 | 40% | | |
| Injection site reaction | 4 | 40% | | |
| Redness (injection site) | 1 | 10% | | |
| Pruritus (injection site) | 3 | 30% | | |
| Respiratory | | | | |
| Pleural effusion | 1 | 10% | | |
| Dyspnoea | 1 | 10% | | |
| Gastrointestinal | | | | |
| Diarrhoea | 2 | 20% | | |
| Constipation | 1 | 10% | | |
| Abdominal pain | 2 | 20% | | |
| Endocrinal | | | | |
| Adrenal insufficiency | | | 1 | 10% |
| Hypophysitis | | | 1 | 10% |
| Skin | | | | |
| Rash | 1 | 10% | | |
| Dry skin | 3 | 30% | | |
| Pruritus | 2 | 20% | | |
| Vitiligo | 1 | 10% | | |
| Laboratory tests | | | | |
| Increased amylase | 2 | 20% | | |
| Hyponatremia | | | 1 | 10% |
| Infusion reaction | | | | |
| Other | | | | |
| Fatigue | 3 | 30% | | |
| Nausea | 3 | 30% | | |
| Xerostomia | 1 | 10% | | |