**Supplementary File 1.** Main characteristics of the cases summarized in the database search.

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|  | Publication (last name, year) | Immune checkpoint inhibitor (ICI) | Indication for ICI | Age (years) | Gender | Timing | Management | Outcome | Other immune related adverse events |
| 1 | Takahashi, 202012 | Pembrolizumab | Lung adenocarcinoma | 78 | Male | 7 days | Intravenous methylprednisolone 1000 mg/day for 3 days (started 46 days after Pembrolizumab dose due to delay in HLH diagnosis). After the pulse steroid therapy, received 60 mg/day (1 mg/kg/day) of prednisolone, which was tapered to 50 mg/day within 4 weeks | Steroid pulse therapy rapidly alleviated fever, rashes, and abnormal laboratory values. | Suspected immune mediated hepatitis |
| 2 | Kalmuk, 202013 | Pembrolizumab | Metastatic head and neck squamous cell carcinoma | 61 | Male | After cycle 14 | Dexamethasone 10 mg/m2 and etoposide 150 mg/m2 | Completed a standard HLH regimen, 3 months later, labs normalized. Restarted on Pembrolizumab 8 months later and no recurrence of HLH at cycle 5. | None |
| 3 | Thummalapalli, 202028 | Nivolumab | Glioblastoma | 74 | Male | On cycle 2, day 17 | Intravenous methylprednisolone followed by oral prednisone | No response, transitioned to comfort measures, patient expired on day 15 of admission | None |
| 4 | Hantel, 201829 | Ipilimumab + Nivolumab | Metastatic melanoma | 35 | Female | Presented 3 weeks after 1st cycle | 1.5 mg/kg of methyl prednisone every 8 hours decreased to 1h/g of oral prednisone She remained on high-dose steroids for 1 month before being tapered slowly down to her prior replacement dose regimen for panhypopituitarism. | Resolution of HLH. | None |
| 5 | Akagi, 202030 | Pembrolizumab | Lung adenocarcinoma | 74 | Male | 7 days | 1,000 mg of high-dose methylprednisolone once followed by dexamethasone 10mg/m2 and etoposide 150mg/ m2 | Of note, developed bone marrow suppression and neutropenic sepsis secondary to etoposide which subsequently resolved. | None |
| 6 | Sadaat, 201815 | Pembrolizumab | Metastatic melanoma | 58 | Male | NA | Oral prednisone administered at 1 mg per kilogram per day. After 5 weeks of steroid dose was tapered over 7 weeks | Resolution of HLH | None |
| 7 | Laderian, 201931 | Pembrolizumab | Metastatic Thymic carcinoma | 49 | Male | 1 year | High dose steroids, anakinra, IVIG | Death | None |
| 8 | Sasaki, 201832 | Dabrafenib and trametinib combination therapy following Pembrolizumab | Metastatic melanoma | 60 | Female | 13 days | Discontinued Dabrafenib and trametinib, initiated prednisolone and later tapered over 5 weeks. 16 days after discontinuation, dabrafenib and trametinib were reintroduced at lower doses and gradually titrated over 4 months without any adverse effects. | Resolution of HLH | None |
| 9 | Okawa, 201833 | Pembrolizumab | Squamous cell carcinoma of the lungs | 78 | Male | 10 days | Started steroid pulse therapy followed by taper. | Resolution of HLH. Continued with treatment after steroids, no disease recurrence | Autoimmune Hemolytic Anemia |
| 10 | Lorenz, 201934 | Pembrolizumab | Castration resistant prostatic cancer with bone-, lymph node- and lung metastases. | 68 | Male | Within a few days | High dose steroids, plasmapheresis, cyclosporin A, etoposide, and tacrolimus. | Resolution of HLH. Nine months after termination of pembrolizumab treatment, the patient remained free of relapse. | None |
| 11 | Ozdemir, 202035 | Ipilimumab + Nivolumab | Metastatic melanoma | 42 | Male | 51 days | High dose corticosteroids with a taper over 30 days | Resolution of HLH, Complete Response from cancer treatment. | Pancytopenia, hepatitis |
|  | Nivolumab | Metastatic melanoma | 36 | Male | 78 days | High dose corticosteroids with a taper over 21 days | Resolution of HLH, Partial Response from cancer treatment. | Pancytopenia, hepatitis |
| Ipilimumab +Nivolumab | Metastatic melanoma | 32 | Male | 91 days | High dose corticosteroids with a taper over 21 days | Resolution of HLH, Partial Response from cancer treatment. | Pancytopenia, hepatitis |
| 12 | Chin, 201914 | Ipilimumab and Nivolumab | Metastatic melanoma | 69 | Female | after 4 cycles | IV methylprednisolone three days (1500 mg daily), followed by oral prednisolone 1 mg/kg/day tapered over two months. | Over six weeks, normalization of ferritin, fibrinogen and cytopenia. | None |
| 13 | Al-Samkari, 201836 | Pembrolizumab | Metastatic breast cancer | 58 | Female | NA | A high-dose methylprednisolone taper (initial dose 1 g, with   slow taper over a few weeks) | Resolution of HLH. | Hypophysitis |
| 14 | Dupre, 202037 | Pembrolizumab | Pulmonary sarcomatoid carcinoma | 58 | Male | 1 week | Prednisone | Partial control of HLH, death from cancer progression | None |
| Nivolumab + Ipilimumab | Metastatic melanoma | 54 | Female | 3 weeks | IV Methylprednisolone 500mg followed by oral prednisone, etoposide 10mg/m2, IVIG 1g/kg, Tocilizumab | Partial control of HLH, cancer progression | None |
|  |  | Pembrolizumab | Metastatic melanoma | 35 | Female | 28 days after Ipilimumab | Prednisone 1mg/kg/day, Etoposide 150mg/m2 intravenous | Death from HLH with intracerebral hemorrhage | Hepatitis |
| Nivolumab + Ipilimumab | Metastatic melanoma | 52 | Male | 5 weeks after Ipilimumab | Corticosteroids 1mg/kg/day | Resolution of HLH, rechallenged with ICI with no recurrence of HLH | Hepatic cytolysis and lymphocytic meningitis |
| Pembrolizumab | Metastatic melanoma | 69 | Male | 4 weeks | Methylprednisolone 100mg/ day | Resolution of HLH, not rechallenged with ICI, cancer response not documented | Hypophysitis, lymphocytic meningitis, hepatic cytolysis |
| 15 | Satzger, 201838 | Nivolumab + Ipilimumab | Metastatic melanoma | 27 | Female | 5 weeks | Prednisone 2mg/kg, later switched to 1.5mg/kg and then tapered, mycophenolate mofetil 360mg twice daily and increased to 720mg twice daily | ICI was discontinued. Laboratory values normalized; clinical symptoms resolved | Thyroiditis |
| 16 | Shah, 201739 | Pembrolizumab | Metastatic bladder cancer | 76 | Male | 9 months | Etoposide and dexamethasone per HLH 2004 protocol | NA | None |