Supplementary table: Extrapolations beyond the US FDA approval and their supporting data.
As of March 25, 2016 for NCCN guidelines and US FDA approvals.

Drug	Extrapolation	Data Supporting Extrapolation
Ixazomib	1. Ixazomib w/ dex after prior therapy 2. Ixazomib alone after prior therapy 3. Ixazomib w/ dex/len as other regimen for transplant candidate (not requiring previous therapy)	1. no link provided 2. PMID 24904120. Phase I trial of 60 patients with multiple myeloma to evaluate safety and tolerability and determine the maximum tolerated dose of single-agent, oral ixazomib given weekly for 3 of 4 weeks. Secondary end point evaluated disease response which was defined based on the International Myeloma Working Group uniform criteria (ref PMID 16855634). Median duration of response for monotherapy was 7.3 months. 3. No link provided
Cobimetinib	1. does not state specific BRAF mutation though approved only for V600E or V600K mutations	1. PMID 25265494. Randomized-control trial of495 patients with previously untreated unresectable locally advanced or metastatic BRAF V600 mutation-positive melanoma to receive vemurafenib and cobimetinib (combination group) or vemurafenib and placebo (control group). The primary end point was investigator-assessed progression-free survival. Combination group had 9-month survival of 81% versus 73% in monotherapy group overall, but study did not stratify based on mutation
Talimogene laherparepvec	1. does not require surgery prior to initiating treatment	1. PMID 26014293. Open label study where patients were assigned in 2:1 ratio to either T-VEC or subcutaneous recombinant GM-CSF, but does not require prior surgery in inclusion criteria (436 patients)
Trifluridine/tipiracil	1. Able to skip all 3 prior therapies (fluoropyrimidine-, oxaliplatin- and irinotecan-based chemotherapy, an anti-VEGF biological therapy, and if RAS wild-type, an anti-EGFR therapy) as specified in FDA indication	1. PMID 25970050. Double-blind randomized control trial of 800 patients with biopsy proven adenocarcinoma of the colon or rectum. 100% of participants had completed fluoropyrimidine-, oxaliplatin- and irinotecan-based chemotherapy, an anti-VEGF biological therapy. 51% had documented KRAS mutation in both treatment or control group, with 52% of treated and 54% of controls received anti-EGFR therapy prior to enrollment. Regardless, all subjects received at least 2 previous therapies

Panobinostat	1. excludes combination requirement for bortezomib and dexamethasone 2. Recommendation for prior treatment does not specify 2 prior regimens including bortezomib and an immunomodulatory agent.	1. No link provided 2. No link provided
Palbociclib	1. treatment of well differentiated liposarcoma for retroperitoneal sarcomas	1. PMID 23569312. Open label phase II trial evaluating progression free survival at 12 weeks in patients with well-differentiated and dedifferentiated liposarcomas with proven CDK4 amplification that concluded benefit because PFS was > 40% at 3 months compared to historical control. (30 patients)
Nivolumab	1. monotherapy for BRAF-wild type 2. renal cell carcinoma that has not received anti-angiogenic therapy 3. used in melanoma without following ipilimumab	1. PMID 23569312. Double-blind randomized controlled trial where patients with stage III melanoma were assigned to either nivolumab monotherapy, nivolumab in combination with ipilimuab, or ipilimumab alone. Results do not report data for nivolumab alone and only reports improved progression free survival for patients receiving combined therapy in regards to BRAF-mutation status. (30 patients) 2. PMID 26406148. Randomized trial of patients with advanced clear-cell renal cell carcinoma that had received one or two regimens of antiangiogenic therapy. Trial does not include patients that were anti-angiogenic therapy naïve (821 patients) 3. PMID 25399552. Randomized trial in patients with unresectable BRAF wild-type melanoma to either nivolumab plus decarbazine-matched placebo or dacarbazine plus nivolumab-matched placebo in patients not previously treated with ipilimumab. Primary end point was overall survival, which was greater in the nivolumab group (418 patients)
Idelalisib	1. Requires only 1 versus 2 prior systemic therapies for patients with follicular B-cell lymphoma 2. Without rituxumab in those without significant comorbidities with CLL	1. PMID 24450858. Open-label phase II trial in patients with indolent non-Hodgkin's lymphoma who had received at least 2 prior therapies (58% had FL). Overall response rate of FL subgroup was 0.54 (0.42-0.66), but no patients in this study received solely 1 systemic therapy prior to enrolling. (125 patients) 2. No link provided

Ceritinib	1. treatment for soft tissue sarcoma	1. No link provided
Ramucirumab	1. Does not require treatment in combination with FOLFIRI for metastatic colorectal cancer 2. No requirement for treatment on or previously with bevacizumab, oxaliplatin, and fluoropyrimidine in colorectal cancer	1. PMID 25877855. Randomized, double-blind, phase III trial in combination with FOLFIRI. No patients were treated with solely irinotecan therapy (1072 patients) 2. No link provided
Obinutuzumab	1. Additional recommendation removes requirement for co-administration of chlorambucil	1. Phase 2 study with 80 patients with a response rate of ~49-67%
Afatinib	1. Indicated as subsequent therapy for adenocarcinoma 2. NSCLC with HER2 mutations	1. No link provided 2. PMID 22325357. Described of 3 cases in patients with lung adenocarcinoma with HER2 mutation who received clinical benefit with afatinib after failing previous therapies. Also article of the prevalence of the mutation.

Trametinib	1. treatment for NSCLC	1. ASCO abstract 8006, 2015 Annual Meeting. Single-arm phase II trial of 24 patients with NSCLC treated with dabrafenib plus trametinib who had failed one prior systemic therapy. Overall response rate of 63% (15/24)
Dabrafenib	1. treatment for NSCLC	1. ASCO abstract 8006, 2015 Annual Meeting. Single-arm phase II trial of 24 patients with NSCLC treated with dabrafenib plus trametinib who had failed one prior systemic therapy. Overall response rate of 63% (15/24)
Radium-223	1. treatment for osteosarcoma	1. PMID 24924181. Book Chapter discuss therapeutic potential of radium-223, but provides no evidence of efficacy in osteosarcoma
Pomalidomide	1. does not specific requirement of 2 prior therapies including lenalidomide and a proteasome inhibitor	1. No link provided. All cited trials included prior therapy of lenalidomide and a proteasome inhibitor

Cabozantinib	1. treatment for kidney cancer 2. NSCLC with RET rearrangement	1. PMID 26406150. Randomized trial of 658 patients with RCC who had progressed on anti-VEGF therapy to either cabozantinib or everolimus with primary endpoint of progression free survival (7.4 months in cabozantinib versus 3.8 months in everolimus). 2. Phase 2 study with <50 people
Ziv-Aflibercept	1. does not require FOLIRI combination, but states irinotecan combination alone is acceptable in colorectal cancer 2. does not specify resistance or progression of colorectal cancer following oxaliplatin-therapy is required	1. No link provided 2. No link provided
Carfilzomib	1. primary therapy for transplant candidates in combination with lenalidomide and dexamethasone, where FDA approval solely for relapsed or refractory disease 2. Alternative regimen recommendation of combination panobinostat with carflizomib 3. treatment for Waldenstrom's macroglobinemia	1. PMID 22665938. Open-label of both transplant-eligible and ineligible patients newly diagnosed with multiple myeloma. Primary end point was safety followed by subgroup enrollment in phase II trial that evaluated rate of at least near-complete response (<5% plasma cells in marrow with detectable MM cells in serum/urine) following 4 cycles of treatment. Phase II showed 62% near-complete response. 24-month PFS was 92% (53 patients) 2. PMID 25710456. Open-label phase I/II trial to determine maximum tolerated dose as well as overall response rate in patients who progressed during or after >1 treatment for MM. 28 of 47 patients had ORR 3. PMID 24859363. Open-label phase II trial with carfilzomib to determine overall response rate in combination with rituximab and dexamethasone. ORR was 87.1% (31 patients)
Pertuzumab	1. in combination with paclitaxel instead of doclitaxel	1. Ongoing trial NCT01276041. Initial findings published in ASCO Annual Meeting Abstract 606. Study enrolled 53 patients, and 29/36 patients had PFS at 6 months

Vismodegib	1. following standard excision of basal cell carcinoma with positive margins requiring Mohs or resection or radiation therapy.	1. PMID 22670903. International two-cohort non-randomized study patients with inoperable disease or where surgery was deemed to be inappropriate. Study does not include patients undergoing multiple surgeries (initial excision followed by Mohs) or radiation (33 patients)
Axitinib	1. first line therapy for stage IV or surgically unresectable RCC. FDA indication following one prior systemic therapy	1. PMID 24140184. Randomized, double-blind phase II trial of patients with RCC that were treatment naive. All patients received axitinib 5 mg twice daily for 4 weeks followed by randomization to either up titration of 7 mg dose or maintained 5 mg dose. Primary outcome was objective response between the two groups (213 patients)
Crizotinib	1. treatment for soft tissue sarcoma 2. removes requirement for locally advanced or metastatic disease 3. Ok for treatment in NSCLC not otherwise specified beyond ALK+ or ROS1+	1. PMID 20979472. Description of two patient case reports 2. No link provided 3. No link provided
Brentuximab vedotin	1. treatment of mycosis fungoides/Sezary syndrome 2. primary treatment in anaplastic large cell lymphoma 3. For non-systemic disease	1. PMID 26261247. Open-label, phase II trial to determine safety and prelim activity in 48 patients with MF or pc-ALCL. Overall response was 54% for patients with MF 2. No link provided 3. No link provided

Vemurafenib	1. Hairy cell leukemia 2. NSCLC 3. Does not specify BRAF V600E mutation	1. PMID 26352686. 2 cohort (Italian and American) open-label trial evaluating complete response rate (Italian) and overall response rate (American) in patients with relapsed or refractory hairy cell leukemia. Overall response rate 96% in Italian cohort and 100% in American cohort (26 patients) 2. PMID 26287849. Patients with non-melanoma BRAF+ malignancies, including 20 with NSCLC were treated with vemurafenib monotherapy. Primary outcome was overall response rate. Response rate was 42% in NSCLC cohort 3. PMID 22356324. Phase II trial of patients with previously treated BRAF V600-mutation metastatic melanoma to evaluate overall response rate of vemurafenib. 7% (9/132) of 132 patients had V600K mutation, while 82% possessed BRAFV600E.
Vandetanib	1. Non-medullary thyroid cancer	1. No link provided