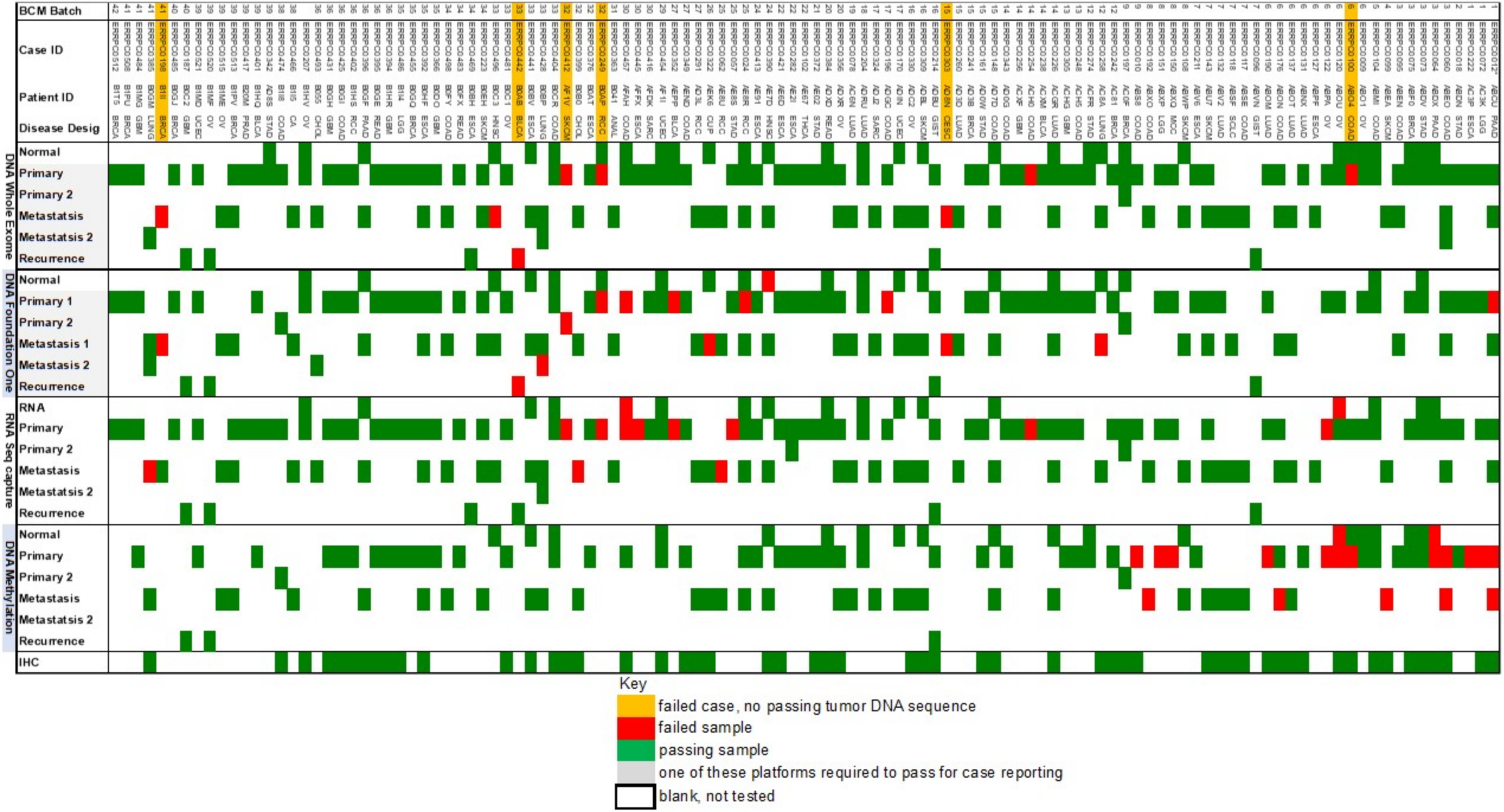
BCM Batch
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DNA Whole Exome
Normal
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RNA Seq capture
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Primary 2
Metastasis
Metastatsis 2
Recurrence
DNA Methylation
Normal
Primary
Primary 2
Metastasis
Metastatsis 2
Recurrence
IHC
Key
failed case, no passing tumor DNA sequence
failed sample
passing sample
one of these platforms required to pass for case reporting
blank, not tested

Supplementary Figure 1. Exceptional responder sample analyte overview. Here we show the samples from which DNA and RNA was isolated for each of the ER cases. Sample analyte evaluation was attempted on 126 subjects. Of 126 subjects 7 were duplicate samples, and 2 were withdrawn from the project with manuscript in revision. To be counted as a valid analysis, at least 1 tumor sample had to have a successful DNA sequence by either whole exome or the FoundationOne panel. Six patients were failed for lack of DNA, but any successful RNAseq from these patients would be kept as controls. Color legend: **Gray** highlight at far right indicates tracks where tumor WES was performed. **Green** cells are successfully sequenced samples, using WES or RNA Seq. **Red** cells samples failed sequencing usually at the library stage. **Orange** highlight indicates specimens in which analyte evaluation was unsuccessful (10 cases failed). 17 normal RNAs were sequenced to furnish controls

Supplemental Table 1: Reviewers for exceptional responder cases

Specialty	Name	Affiliation
Medical Oncology	Barbara A. Conley MD	Division of Cancer Treatment and Diagnosis, NCI
Medical Oncology	JoAnne Zujewski MD	Division of Cancer Treatment and Diagnosis, NCI
Pediatric/Medical Oncology	S. Percy Ivy, MD	Division of Cancer Treatment and Diagnosis, NCI
Medical Oncology	Naoko Takebe MD	Division of Cancer Treatment and Diagnosis, NCI
Medical Oncology	Jeffrey White MD	Division of Cancer Treatment and Diagnosis, NCI
Medical Oncology	Geraldine O'Sullivan-Coyne MD	Developmental Therapeutics Clinic, NCI
Medical Oncology	Elise Kohn, MD	Division of Cancer Treatment and Diagnosis, NCI
Medical Oncology	Richard Little MD	Division of Cancer Treatment and Diagnosis, NCI
Medical Oncology	Shakun Malik, MD	Division of Cancer Treatment and Diagnosis, NCI
Medical Oncology	Lyndsay Harris, MD	Division of Cancer Treatment and Diagnosis, NCI
Medical Oncology	Bhupinder Mann, MD	Division of Cancer Treatment and Diagnosis, NCI
Pathology	Irina Lubensky MD	Division of Cancer Treatment and Diagnosis, NCI
Molecular Oncology	Jean-Claude Zenklusen PhD	Center for Cancer Genomics, NCI
Molecular Oncology	Paul M. Williams, PhD	Frederick National Laboratory for Cancer Research, Frederick MD
Molecular oncology	James V. Tricoli PhD	Division of Cancer Treatment and Diagnosis, NCI
Molecular Oncology	Roy Tarnuzzer PhD	Center for Cancer Genomics, NCI
Molecular Oncology	Chris Karlovich, PhD	Frederick National Laboratory for Cancer Research, Frederick MD
Radiology and Nuclear Medicine	Brian Rodgers MD	Division of Cancer Treatment and Diagnosis, NCI
Ethics	Carol Weil JD	Division of Cancer Treatment and Diagnosis, NCI

Supplemental Table 2: categories of consent for patients who had died or had been lost to follow-up

Category	Requirements	Use of tissue for ER?
1	Patient (currently either alive or deceased) previously indicated in a consent form (at the time the tissue that will be used for the Exceptional Responders Initiative was collected) that his or her tissue and data could be used for *future medical or disease research*	YES, this *tissue and associated medical data may be used.* *Justification:* Current cutting-edge scientific research across all diseases includes investigation of the molecular biology of the disease through "omic" sequencing of tissue to determine underlying causal mutations. The Exceptional Responder's Initiative is sequencing samples to find the potential underlying characteristics of a tumor that led a patient to have an exceptional response to an agent that failed to produce a response in most other patients.
2	Patient (currently either alive or deceased) previously indicated in a consent form that his or her tissue could be used for *future cancer research*.	YES, this *tissue and associated medical data may be used.* *Justification:* The current state of cancer research has a strong focus on developing targeted agents and providing personalized medicine to treat patients. As cancer is a disease of the genome, permission to use tissue and data for cancer research logically includes permission to conduct the genome sequencing contemplated in this study.
3	Patient (currently alive) had not previously indicated that his or her tissue could be used for future research, but indicated he or she could be re-contacted	MAYBE, if *patient is alive,* attempt will be made to contact the patient and consent will be sought for this study with the Exceptional Responders Initiative consent form. If the patient consents to have his or her tissue used for this study, the *tissue and case would be included* as part of this study. If the patient refuses consent for this study, his or her tissue would not be included. If the patient is lost to follow-up, the IRB may consider waiving consent *Justification:* Patient gave permission to be re-contacted for potential inclusion in future studies. If patient is re-contacted and agrees to be included in this study, he or she will have done so knowing the full details of the study as conveyed in the informed consent. If it is impracticable to contact the patient, it may be possible to waive consent. NO, if the *patient is deceased*, this case would not be included in the Exceptional Responders Study. *Justification:* These patients did not want their tissue used without being provided a specific opportunity to be informed of future research studies and to decide based on that specific study information whether to participate. Therefore, it would be unethical to use

		such patients' tissue for ER or try to re-contact their family members.
4	Patient (currently alive or deceased) had previously indicated in prior consents that their *tissue could not be used for future cancer* or disease research and that they could not be re-contacted	NO, their tissue and *case would not be included* as part of this study. *Justification:* Patient did not want their tissue used for any future research and did not want to be contacted.
5	*Patient is deceased*; prior consent did not indicate whether the tissue collected could be used for future research. The prior consent also did not indicate whether the patient could be re-contacted.	YES, tissue may be used for this project. *Justification:* Patient is deceased so secondary use would not constitute human subject research. In addition, use of the tissue does not violate a known preference of the patient regarding re-contact or regarding any limitations on use of the tissue for research purposes.
6	*Patient is alive;* prior consent did not indicate whether the tissue collected could be used for future research. The prior consent also did not indicate whether the patient could be re-contacted.	MAYBE, the patient would be contacted if possible and asked for his or her consent to use tissue for this study. If the patient consents to have his or her tissue used for this study, the *tissue and case would be included* as part of this study. If the patient refuses to consent for this study, the patient's *tissue would not be included*. If the patient cannot be reached, waiver of informed consent would be requested to use the tissue. *Justification:* If patient is alive, it is considered human subjects research and the patient will need to provide consent for this study, or else an IRB may waive consent under 45 CFR 46.116(d)[1], If a patient cannot be reached after an effort to re-contact is made, the research meets the criteria for waiver set forth under 45 CFR 46.116(d).

Supplemental Table 3: Type and duration of exceptional response (complete response (CR) or partial response (PR)) in 117 patients

Ordinal list of cases by tumor type	Age range, sex	Tumor	Treatment Regimen	Response and duration	Clinical trial	Additional clinical information	Type of ER
Colorectal cancer							
1	70-80, F	Metastatic colon adenocarcinoma	irinotecan bevacizumab	CR 22+ months	No	MSI-H; pelvic mesenteric implant 7 months post-surgery + adjuvant chemotherapy	Expected CR rate < 10% (21)
2	50-60, M	Metastatic colon adenocarcinoma	5-fluorouracil leucovorin oxaliplatin bevacizumab and cyto-reductive surgery with mitomycin C HIPEC	CR 9 + months	No	Metastases at initial diagnosis in lung, liver, adrenal; extensive adenopathy; large cecal mass; peritoneal metastases	CR< 10% expert opinion of reviewers
3	40-50, F	Metastatic colon adenocarcinoma	5-fluorouracil leucovorin oxaliplatin bevacizumab	CR 14 months	NCT 00070122	Liver metastases	Expected CR rate < 10% (22)
4	50-60, F	Metastatic colon adenocarcinoma	irinotecan capecitabine bevacizumab	CR 24 months	No	Pelvic mass	Expected CR rate < 10% (23)
5	50-60, M	Metastatic colon adenocarcinoma	5-fluorouracil leucovorin oxaliplatin bevacizumab	CR 112 months	No	Liver metastases	Expected CR rate < 10% and response duration > 3 x published median (7.3 months) (22)
6	50-60, F	Metastatic colon adenocarcinoma	irinotecan 5-fluorouracil leucovorin bevacizumab	CR 75 months	No	Hilar nodes, retroperitoneal adenopathy; lung nodules	Expected CR rate < 10% and response duration > 3X median progression

							free duration (10.6 months) (24)
7	60-70, M	Metastatic colon adenocarcinoma	5-fluorouracil + leucovorin (change to capecitabine) oxaliplatin bevacizumab	CR 66 months	No	Peritoneal nodules; hilar masses	Expected CR rate < 10% and response duration > 3x published median (7.3 months). (22, 25)
8	60-70, F	Metastatic colon adenocarcinoma	5-fluorouracil leucovorin, oxaliplatin bevacizumab	CR 9 months	No	Metastases left hilum, liver, abdominal nodes	Expected CR rate < 10% (22)
9	40-50, F	Metastatic colon adenocarcinoma	capecitabine oxaliplatin bevacizumab	CR 49 months	On clinical trial; trial too old to have NCT number	Prior treatment HIPEC + debulking; progressed with multiple liver metastases	Expected CR rate < 10% and response duration > 3x published median (9.6 months) (26)
10	60-70, M	Metastatic colon adenocarcinoma	5-fluorouracil leucovorin oxaliplatin bevacizumab	CR 54 months	No	Multifocal liver and nodal metastases; *KRAS* mutation	Expected CR rate < 10% and response duration > 3x published median (9.4 months) (27)
11	50-60, F	Metastatic colon adenocarcinoma	5-fluorouracil leucovorin irinotecan bevacizumab	CR 48 months	No	Supraclavicular and retrocaval adenopathy 2nd line	Expected CR rate < 10% and response duration > 3x published median (3.2 months) (28)
12	60-70, M	Metastatic colon adenocarcinoma	5-fluorouracil leucovorin oxaliplatin	CR 5 months	No	Liver metastases	Expected CR rate < 10%. (29)

			cetuximab				
13	60-70, F	Metastatic colon adenocarcinoma	5 cycles: 5-fluorouracil leucovorin oxaliplatin Then Exploratory laparotomy, debulking showing no evidence of disease, mitomycinC intraperi-toneal chemo-therapy	CR 13 months	No	Peritoneal metastases; CR after 4 cycles of 5-fluorouracil, leucovorin, oxaliplatin	Expected CR rate < 10% (30)
14	60-70, F	Metastatic colon adenocarcinoma	5-fluorouracil leucovorin oxaliplatin irinotecan bevacizumab	CR 40 months	No	Liver metastases at diagnosis; right hepatectomy after chemotherapy; long periods without progression but had several local treatments for oligo-metastases to liver and lung	Expected CR rate < 10%. (31,32)
15	60-70, M	Metastatic colon adenocarcinoma	capecitabine 5 years	CR 128 months	On clinical trial (1997); trial too old to have NCT number	Liver metastases	Expected CR rate < 10% and response duration > 3x published median (5.2 months) (33)
16	40-50, F	Metastatic rectal adenocarcinoma	5-fluorouracil leucovorin oxaliplatin bevacizumab x 7 months followed by radiotherapy / capecitabine followed by capecitabine +	CR 26 months	No	Liver metastasis	Expert opinion: expected CR rate < 10% (primary and metastatic disease) (34)

			bevacizumab X 3 months followed by resection with no pathologic evidence of disease				
17	40-50, M	Rectal adenocarcinoma	5-fluorouracil leucovorin oxaliplatin bevacizumab then maintenance bevacizumab	CR 52 months	No	Prior treatment with neoadjuvant Chemo-radiotherapy and excision; Subsequent increase in CEA with increased external Iliac and inguinal adenopathy; Stopped oxaliplatin for neurotoxicity	Expected CR rate < 10% (35)
18	60-70, F	Metastatic colon adenocarcinoma	5-fluorouracil leucovorin oxaliplatin bevacizumab	PR 122 months	No	Liver metastases; Abdominal lymphadenopathy 2 months post curative resection of primary tumor	Response duration > 3x published median (7.3 months) (22)
19	50-60, M	Metastatic colon adenocarcinoma	5-fluorouracil leucovorin oxaliplatin cetuximab	PR 53 months	NCT 00265850	Liver metastases; Abdominal lymphadenopathy	Response duration > 3x published median (12.3 months) (29)
20	60-70, M	Metastatic colon adenocarcinoma	temozolo-mide TRC102 (methoxy-amine hydro-chloride	PR 27 months	NCT 01851369	Lung metastases; retroperitoneal and supraclavicular adenopathy	Response duration longer than expected (2-3 months). Expert opinion, no published data
21	70-80, M	Metastatic colon adenocarcinoma	capecitabine	PR 26+ months	No	8 months post resection; lung metastases and subcutaneous metastases	Response duration > 3x published median (7.2 months) (33)

22	20-30, F	Metastatic colon adenocarcinoma	irinotecan fluorouracil leucovorin first with bevacizumab then with cetuximab	PR 18 months (potential CR with imaging abnormalities)	NCT 00911170 On protocol only 2 months (evaluation of pegfigras-tim only)	MSS; no *KRAS* mutation; Massive Liver metastases; chemotherapy duration 3 months	Expected CR rate < 10% Median published PFS 10.4 months (24)
Gastro-esophageal cancer							
23	70-80, M	Metastatic gastroesophageal adenocarcinoma	MK-2206	CR 15 months	NCT 01260701	2nd line liver metastases; peripancreatic adenopathy	Published CR rate < 1% (36)
24	60-70, M	Metastatic gastroesophageal adenocarcinoma	paclitaxel carboplatin	CR 104 months	No	Liver metastases 9 courses of chemotherapy then stopped.	Response duration > 3 x published median (5.3 months) (37-n)
25	50-60, M	Metastatic gastroesophageal adenocarcinoma	cisplatin 5-fluorouracil epirubicin oxaliplatin capecitabine	CR 49 months	No	Metastasis to right supraclavicular, mediastinal and retroperitoneal nodes	Expected CR rate < 10% (38)
26	70-80, M	Metastatic gastroesophageal adenocarcinoma	5-fluorouracil leucovorin oxaliplatin	CR 22+ months	No	Liver metastases	Expected CR rate is < 10% and response duration > 3 x published median (6 months in patients > 65 years) (39)
27	60-70, M	Metastatic gastroesophageal adenocarcinoma	capecitabine oxaliplatin epirubicin	CR 40 months	No	Liver metastases	Expected CR rate < 10% (38)
28	40-50, M	Metastatic gastroesophageal adenocarcinoma	cisplatin capecitabine trastuzumab	CR 50 months	No	*ERBB2* amplification Lymphadenopathy	Expected CR rate < 10% and response duration > 3X published median PFS (6.7 months) (40)

29	50-60, M	Metastatic gastroesophageal adenocarcinoma	oxaliplatin capecitabine epirubicin	CR 12 months	No	HER2 IHC 3+ Metastatic brain, liver, subcarinal, gastro-hepatic nodes. Patient presented with brain metastasis	Expected CR rate < 10% (38)
						which were resected followed by whole brain radiotherapy; patient received definitive radiotherapy and concurrent weekly cisplatin + irinotecan to primary, followed by epirubicin, oxaliplatin and capecitabine	
30	60-70, M	Metastatic gastroesophageal adenocarcinoma	5-fluorouracil leucovorin oxaliplatin	CR 25 months	No	*ERBB2* amplified; Metastasis to bone, liver, retroperitoneal and mediastinal lymph nodes	Expected CR rate is < 10% and response duration > 3X published median PFS (6.7 months)(39)
31	60-70, M	Metastatic gastroesophageal adenocarcinoma	capecitabine oxaliplatin	CR 55 months	No	2nd line recurrent metastatic disease HER2 negative by IHC and FISH;	Expected CR rate < 10% and response duration > 3X published median PFS (6.7 months) (39,41)
32	40-50, M	Metastatic gastroesophageal adenocarcinoma,	5-fluorouracil leucovorin oxaliplatin trastuzumab	CR 13 months	No	*ERBB2* amplification; retroperitoneal adenopathy	Expected CR rate < 10% (40)
33	50-60, M	Metastatic gastroesophageal adenocarcinoma	5-fluorouracil leucovorin oxaliplatin trastuzumab	PR 20 months	No	*ERRB2* amplification; liver metastases.	Response duration > 3X published median (6.7 months) (40)

34	70-80, F	Metastatic gastroesophageal adenocarcinoma	5-fluorouracil leucovorin oxaliplatin	PR 13 + months	NCT 01498289	Liver metastases	Response ongoing, duration nearly 3 x published median (5.8 months) (39)
35	40-50, M	Metastatic gastroesophageal adenocarcinoma	5-fluorouracil leucovorin oxaliplatin	PR 24+ months	No	HER2 expression negative; Lung metastases; para-aortic lymphadenopathy	Response duration > 3 x published median (5.8 months) (39)
36	70-80, M	Metastatic gastroesophageal adenocarcinoma	5-fluorouracil leucovorin oxaliplatin vismodegib	PR 21 months	NCT 00982592	Liver metastases	Response duration > 3 x published median (5.8 months) (39)
37	60-70, M	Metastatic gastroesophageal adenocarcinoma	docetaxel cisplatin radiation	PR 128 months	No	Lymphadenopathy ; Tumor recurred and again treated with chemo-radiation	Response duration > 3x published median (24 months) (42)
38	70-80, M	Metastatic gastroesophageal adenocarcinoma	5-fluorouracil leucovorin irinotecan	PR 14 months	No	HER2 IHC 1+ 2ND line	Response duration > 3 x expected (expert opinion)
39	60-70, M	Metastatic gastroesophageal adenocarcinoma *ERBB2* normal	5-fluorouracil leucovorin oxaliplatin	PR 17 months	No	HER2neu IHC 1+ liver metastasis; lymphadenopathy	Response duration > 3 x published median (5.8 months) (39)
40	50-60, F	Metastatic gastroesophageal adenocarcinoma	5-fluororuacil oxaliplatin leucovorin	PR 40 months	No	No *ERRB2* amplification; Liver metastases; mild lymphaden-opathy; gamma knife to brain metastases	Response duration > 3x published median (5.8 months) (39)
Lung Cancer							

41	50-60, F	Metastatic lung adenocarcinoma	docetaxel bevacizumab	CR 39 months	No	4th line treatment; pulmonary metastases	Expected CR rate < 10% and response duration > 3X published median PFS (5.9 months)(43)
42	80-90, M	Metastatic lung adenocarcinoma	carboplatin pemetrexed and pemetrexed maintenance	CR 28 months	No	Lung mass; lymphadenopathy	Response duration > 3X published median duration (4.44 months) (44)
43	60-70, M	Metastatic lung adenocarcinoma	afatinib	CR 4 months	No	1st line; deletion *EGFR* exon 19; bone metastases;	Expected CR rate < 10% (45)
44	60-70, M	Lung adenocarcinoma	paclitaxel pemetrexed bevacizumab	CR 69 months	No	Right upper lobectomy prior to chemotherapy; Recurrent: lymphadenopathy	Expected CR rate < 10% and response duration > 3x published median PFS (8 months)(46)
45	40-50, F	Metastatic lung adenocarcinoma	paclitaxel carboplatin bevacizumab erlotinib	CR 129 months	No	Lung mass; hilar adenopathy KRAS mutation neg EGFR mutation neg *ALK* and *ROS* translocation neg	Expected CR rate < 10% and response duration > 3X published median time to progression for similar regimen (23.7 weeks)(47)
46	60-70, F	Metastatic lung squamous cancer	paclitaxel carboplatin	CR 41 months	No	Left upper lobe lung mass; renal mass; liver metastasis; pelvic mass	Expected CR rate < 10% and response duration > 3X published PFS (5.6 months)(48)
47	40-50, F	Large cell neuroendocrine carcinoma of lung	carboplatin etoposide	CR 65 months	No	Lung and mediastinal masses	Response duration > 3X published median (6.1-7.7 months) (49)

48	50-60, F	Metastatic lung adenocarcinoma	cisplatin pemetrexed	PR 61 months	No	Mediastinal and liver metastases; brain metastasis at 35 months, treated	Response duration > 3x published median (4.1 months) (50)
49	50-60, F	Metastatic lung adenocarcinoma	carboplatin pemetrexed	PR 50 months	No	Prior brain radiotherapy for metastasis; lung mass; right hilar nodes and liver metastases	Response duration > 3x published median (4.1 months) (50)
50	50-60, M	Metastatic lung adenocarcinoma	cisplatin pemetrexed bevacizumab	PR 36 months	No	Ileocecal mass; liver metastasis; hilar mass; adrenal metastasis; colectomy provided pathology	Response duration > 3x published median (6-7.4 months) (51,52)
51	50-60, M	Extensive small cell lung cancer	cisplatin etoposide	PR 27 months	No	Large right infra-hilar mass; chest lymphadenopathy ; few pulmonary masses; rib metastasis	Response duration > 3x published median (5.2 months) (53)
Gynecological Cancer							
52	40-50, F	Papillary serous ovarian cancer	docetaxel trabectedin	CR 18 months	NCT 00569673	Peritoneal carcinomatosis	Expected CR rate < 10% (54)
53	50-60, F	Serous adenocarcinoma of ovary	paclitaxel carboplatin bevacizumab	CR 81 months	NCT 00262847	Germline *BRCA1* mutation; Liver metastases; pelvic masses; retroperitoneal masses	Response duration > 3X published median (13.8 months) (55)
54	80-90, F	Ovarian cancer NOS	paclitaxel carboplatin	CR 69 months	No	Stage IIIC Adjuvant to surgery	Response duration > 3X published median (19 months) (56)

55	60-70, F	High grade serous papillary ovarian cancer Stage IIIB	paclitaxel carboplatin	CR 37 months	NCT 00108745	Adjuvant to surgery	Response duration potentially >3x median published PFS (10-18 months) (56)
56	20-30, F	Serous papillary ovarian cancer	bortezomib	PR 19 months	NCT 00023712	Liver metastasis; pelvic lymph nodes	Partial response rate < 10% for this study (57)
57	20-30, F	Serous papillary ovarian	bevacizumab	PR 63 months	No	4th line; pleural, lung, liver metastasis	Response duration > 3x published median (4.7 months) (58)
58	30-40, F	Metastatic granulosa cell cancer of ovary	temozolo-mide TRC102 (methox-amine hydro-chloride)	PR 20 months	NCT 01851369	7 prior systemic treatments and several prior surgeries; liver metastases	No published data; response duration considered > 3X median reported on clinical trials in patients with multiple prior treatments (2-3 months) Expert opinion
59	40-50, F	Metastatic granulosa cell cancer of ovary	temozolo-mide TRC 102 (methox-amine hydro-chloride)	PR 10 months	NCT018513 69	5 prior systemic treatments; bulky abdominal and pelvic masses	No published data; response duration considered > 3X median reported on clinical trials in patients with multiple prior treatments (2-3 months) Expert opinion

60	40-50, F	Small cell carcinoma ovary	vinblastine bleomycin cyclophos-phamide doxorubicin etoposide	CR 90 months	No	Stage IIIC; complete surgical debulking and 7 cycles of chemotherapy	Response duration > 3x median published survival (approximately 3 years with intensive chemotherapy) (59)
61	50-60, F	Metastatic Endometrial papillary adenocarcinoma	paclitaxel carboplatin	CR 28 months	No	Abdominal and pelvic masses; liver metastasis; retroperitoneal adenopathy	Expected CR rate < 10% and Response duration considered exceptional (expert opinion) (60, 61)
62	50-60, F	Metastatic endometrial endometrioid carcinoma	paclitaxel carboplatin temsirolimus	CR 70 months	NCT 00977574	Pelvic mass; widespread lymphadenopathy	Response duration > 3x longer than expected (expert opinion – median PFS 20 months for paclitaxel, carboplatin and bevacizumab) (62)
63	70-80, F	Metastatic endometrial endometrioid carcinoma	paclitaxel nilotinib	PR 7 months	NCT 02379416	4th line; Lung metastases	Expected PR rate < 10% when patient had no response to prior 3 chemotherapy regimens (expert opinion)

64	60-70, F	Metastatic high grade papillary serous carcinoma fallopian tube	paclitaxel carboplatin	CR 75 months	No	Chemotherapy given after 3rd debulking surgery; No evidence of disease at scan slightly more than a year post end of chemotherapy and at last visit approximately 7 years post chemo	Response duration > 3x published median (10.4 months) (63)
65	30-40, F	Squamous carcinoma cervix	cisplatin gemcitabine	CR 111 months	No	Biopsy proven right hilar mass	Expected CR rate < 10% (64)
66	60-70, F	Leiomyosarcoma of uterus	docetaxel gemcitabine	CR 40+ months	No	ER+; Lung metastases	Expected CR rate < 10% (65)
CNS tumors							
67	30-40, M	oligoastrocytoma	irinotecan	CR 56 months	No	WHO grade III; recurrent; 1p, 10q deletions; no change to slight growth through 5 previous treatment regimens; irinotecan was 6th regimen; slow decrease in size over time over 6 years	Expected CR rate < 10% (66)
68	20-30, F	Glioblastoma multiforme	irinotecan bevacizumab	CR 83 months	No	Stable imaging for 6 years	Expected CR rate < 10% and duration of survival > 3X published median (8.7 mos)(67)
69	20-30, F	Glioblastoma multiforme	cabozantinib	CR 60 months	NCT 01068782	Stable imaging for 5 years	Expected CR rate < 10%; Duration PFS > 3X published median(3.7 months) (68)
70	60-70, F	Recurrent glioblastoma multiforme	cediranib cilengitide	CR 70 months	NCT 00979862		Expected CR rate < 10%; Duration of survival > 3X published

							median (6.5 months) (69, 70)
71	20-30, F	Glioblastoma multiforme	temozolo-mide radiotherapy	CR 117 months	No	Subtotal resection; radiation and adjuvant temozolomide	Response duration > 3X published median survival (13.4 months) (71)
72	70-80, M	Glioblastoma multiforme	temozolo-mide and radiotherapy	CR 49 months	NCT 01062399	Temozolomide adjuvant; gross total resection and radiotherapy	Response duration > 3x published median survival (71)
73	30-40, M	Glioblastoma multiforme	irinotecan temozolo-mide	CR 145 months	NCT 00099125	Adjuvant to gross total resection and radiotherapy	Response duration > 3x published median survival (71)
74	40-50, F	Anaplastic oligo-astrocytoma	irinotecan bevacizumab	PR 95 months	No	2nd line; recurrent after chemoradiation and surgery; deletion 1p36 in 38% of cells and deletion 19q13 in 38% of cells	Response duration > 3 x published median PFS (4.2 months) (67)
75	70-80, M	Glioblastoma multiforme	temozolo-mide	PR 100 months	No	Adjuvant temozolomide; resection + carmustine implant + radiotherapy	Response duration > 3x published median survival (4.7 months) (72)
76	50-60, M	Glioblastoma multiforme	temozolo-mide	PR 162 months	No	Recurred after resection + carmustine implant + radiotherapy; gross total resection + carmustine implant + radiotherapy and temozolomide.	Response duration > 3x published median PFS (4.7 months) (72)

Breast cancer							
77	50-60, F	Metastatic breast adenocarcinoma	carboplatin docetaxel trastuzumab	CR 73 months	No	1st line ER negative, PR negative, *ERBB2* amplified; liver metastases	Response duration > 3x published median (12.4-14.4 months) (73, 74)
78	50-60, F	Breast adenocarcinoma	paclitaxel trastuzumab and capecitabine consolidation	CR 86 months	No	Prior resection and adjuvant chemotherapy and radiation; ER negative, PR negative, HER2 IHC 3+; Recurrent: pulmonary metastases; lymph node metastases	Response duration > 3X median published PFS (12.4 months) (74)
79	60-70, F	Breast adenocarcinoma	docetaxel trastuzumab letrozole	CR 82 months	No	1ST line ER positive, PR positive, *ERBB2* amplified; Liver metastasis	Response duration > 3X median (12.4 – 14.4 months) (74)
80	53-60, F	Metastatic breast adenocarcinoma	trastuzumab pertuzumab	CR 36 months Duration	NCT 01615068 Registry	ER+, PR+, *ERBB2* amplified by FISH Lung and para-mediastinal masses; hilar adenopathy; breast mass	Expected CR rate < 10% (75)

1	50-60, F	Metastatic breast adenocarcinoma	capecitabine (discontinued after 3 months - intolerant) vinorelbine	CR 20 months	No	ER+, PR+, HER2 negative; had adjuvant chemotherapy and aromatase inhibitor; Liver metastases developed within 3 years; biopsy showed ER, PR and HER2 negative	Expected CR rate < 10% (76)
82	40-50, F	Metastatic breast adenocarcinoma	trastuzumab	CR 113+ months	No	Metastatic at presentation ER neg; PR+, HER2 amplified by FISH; Liver metastasis (biopsy proven)	Expected CR rate < 10% and response duration > 3X published median time to progression (18.8 months)(77)
83	50-60, F	Metastatic breast adenocarcinoma	Cyclophos-phamide docetaxel anastrazole zoledronic acid	PR 59 months	No	1st line; ER/PR positive, HER-2 negative, Ki-67 44%; Oncotype recurrence score 18; bone metastases; lung metastases; breast masses	Response - duration > 3x published median (13.1 months) (78)
84	60-70, F	Metastatic breast adenocarcinoma	bevacizumab letrozole	PR 87 months	NCT 00601900	ER and PR positive; lung and bone metastases	Response duration > 3x published median (20.2 months) on this study (79)

85	60-70, F	Metastatic breast adenocarcinoma	capecitabine trastuzumab	PR 50 months	No	2 primary breast cancers, Metastatic to bone and liver at time of treatment	Response duration > 3x published median (14.4 months) (73)
86	60-70, F	Metastatic breast adenocarcinoma	trastuzumab	PR 32 months	No	ER+, PR negative *ERBB2* amplified; Bone metastases; breast mass; axillary adenopathy	Response duration longer than expected (18.8 months) (77)
Melanoma							
87	30-40, F	Metastatic melanoma	paclitaxel carboplatin bevacizumab	CR 66 months	No	2nd metastatic recurrence; treated with resection and adjuvant interferon after 1st recurrence; Developed hilar nodes and lung metastasis; *BRAFV600* mutation	Expected CR rate < 10% and response duration > 3X median PFS (6 months) (80)
88	70-80, F	Metastatic melanoma	dacarbazine	CR 23 months	NCT 00864253	Lung metastases	Expected CR rate < 10% and response duration > 3X published median PFS (1.6 months)(81)
89	80-90, M	Metastatic melanoma	ipilimumab	CR 4 months	No	No *BRAF* mutation; Bone and liver metastases	Expected CR rate < 10% (82)
90	50-60, M	Metastatic truncal melanoma	Ipilimumab	CR 37+ months	No	Adjuvant high dose interferon previously; Developed solitary liver metastasis; disappeared on ipilimumab	Expected CR rate < 10% (82)
91	70-80, M	Metastatic melanoma	ipilimumab	PR 39 months	No	No BRAF mutation; Pelvic and retroperitoneal lymph nodes; liver metastases	Response duration > 3 x published median (12-13 months) (82)

92	60-70, M	Metastatic melanoma	ipilimumab	PR/near CR; 19 months	No	*BRAF* mutation; Subcutaneous and skin metastases	Expected response rate < 10% (82)
Renal cancer							
93	40-50, F	Metastatic clear cell carcinoma kidney	sunitinib	CR 25 months	No	Lung metastases and brain metastases (resected prior to treatment); subcarinal and hilar adenopathy; Chest wall metastases; abdominal metastases (diaphragm)	Expected CR rate < 10% (83)
94	70-80, M	Metastatic clear cell carcinoma kidney	sunitinib	CR 74 months	No	Local progression and lung metastases	Expected CR rate < 10%; response duration >3x published median PFS (11 months) (83)
95	60-70, M	Renal cell carcinoma, NOS	atezolizumab bevacizumab	CR 19 + months	NCT 01984242	Lung and supraclavicular node metastases	Expected CR rate < 10% (84)
96	70-80, M	Metastatic clear cell carcinoma of kidney	temsirolimus	PR 11 months	No	Lung and bone metastases	Response duration > 3X published median PFS (3.8 months) (85)
97	40-50, M	Renal cell carcinoma NOS	everolimus	PR 37 months	No	Mass duodenum/head of pancreas biopsy proven metastasis	Response duration > 3x median published (7.9 months) (86)
Urothelial cancer							
98	50-60, M	Metastatic bladder cancer (urothelial)	Belinostat	CR 12 + months	NCT 01317927	Mediastinal adenopathy	CR rate on this trial < 10% (87)

99	40-50, F	Metastatic bladder cancer (urothelial)	cisplatin gemcitabine cetuximab	CR 75 + months	NCT 00645593	*HRAS* mutation; Lung and liver metastases cetuximab added after progression on gemcitabine and cisplatin, per protocol	Expected CR rate < 10% and response duration > 3X published PFS (7.6 months)(88)
100	70-80, M	Metastatic bladder cancer (urothelial)	nivolumab	CR 16+ months	NCT 02387996	Locally advanced and liver metastases	Expected CR rate < 10% (89)
101	50-60, M	Metastatic bladder cancer (urothelial)	paclitaxel carboplatin focal radiation	CR 64 months	No	Retroperitoneal lymphadenopathy Small cell undifferentiated carcinoma	Response duration > 3x published median (mean survival 6–34.9 months) (90, 91)
Pancreatic cancer							
102	60-70, M	Pancreas adenocarcinoma with squamous metaplasia	5-fluorouracil leucovorin oxaliplatin irinotecan	CR 50 months	No	1st line; Retroperitoneal and mesenteric lymphadenopathy ; porta hepatis mass; Chemotherapy duration 3 months	Expected CR rate < 10% and duration of response > 3x published PFS (6 months)(92)
103	70-80, F	Metastatic pancreatic adenocarcinoma	5-fluoruracil leucovorin oxaliplatin	CR 31 months	No	1st line; Pancreatic mass and biopsy proven liver metastasis; Surgery after chemotherapy found no evidence of malignancy	Expected CR rate < 10% (93)
104	50-60, M	Metastatic pancreatic adenocarcinoma	capecitabine	PR 36 months	No	Found to have liver metastases at curative surgery; this was resected; started adjuvant capecitabine and had 3 years until recurrence	Response duration > 3x expected (expert opinion, extrapolating from published data) (94)
Other cancers							

105	70-80, M	Unknown primary, "favor" bile duct carcinoma	cisplatin gemcitabine	CR 20 months	No	Liver metastases; thoracic, supraclavicular and retroperitoneal adenopathy	Expected CR rate < 10% (96) .
106	60-70, M	Cholangio-carcinoma	cisplatin then carboplatin gemcitabine	CR 21 months	No	Locally advanced disease; mediastinal, supraclavicular, mesenteric and retroperitoneal adenopathy; Patient had only 3 months of cisplatin/carboplatin	Expected CR rate < 10% (97)
107	50-60, M	Metastatic small cell cancer of colon	cisplatin etoposide	CR 59 months	No	Liver metastases; right lower quadrant abdominal mass; peritoneal metastases, soft tissue mass anterior to duodenum	Response duration > 3x the duration of response published. (99, 100)
108	50-60, F	Metastatic anal cancer, squamous	capecitabine	PR 38 months	No	2nd line Recurrent after chemoradiation with mitomycin C; Liver and lung metastases	Response duration > 3X published median (3.2 months for 2nd line chemotherapy) (101)
109	70-80, F	Gastro-intestinal Stromal tumor (GIST)	sunitinib	CR 8 months	No	Recurrent post resection and adjuvant imatinib; Right lower quadrant abdominal mass; mesenteric adenopathy; peritoneal metastases	Expected CR rate < 10% (102)

110	30-40, F	Gastro-intestinal Stromal tumor (GIST)	Imatinib	CR 106 months	No	Abdominal and pelvic metastases; PR to imatinib on recurrence;	Expected CR rate < 10% and response duration >3X published time to progression (24 months) (103)
111	50-60, M	Metastatic papillary thyroid cancer	PF-03084014 (gamma secretase inhibitor)	CR 80 months	NCT 00878189	Lung and paratracheal metastases	Patient was only complete responder and was treated at the lowest dose in this phase I trial (104)
112	60-70, M	Merkel cell cancer, skin	topotecan	PR 33 months	No	Liver and bone metastases Prior cisplatin/carboplatin	Response duration > 3x published median (2-3 months) (105)
113	60-70, M	head/neck squamous carcinoma	5-fluorouracil carboplatin cetuximab	CR 18 months	No	1st line; p16+; Biopsy proven bone metastasis at diagnosis; No radiotherapy	Response duration > 3x published median (5.6 months) (106)
114	40-50, F	Metastatic oropharynx squamous cell carcinoma	docetaxel cisplatin bevacizumab	CR 53 months	NCT 00588770	p16+; Prior definitive chemoradiation with cisplatin; Lung metastases; mediastinal adenopathy	Response duration > 3x published median (6-10 months) (107)
115	70-80, M	Adenocarcinoma unknown primary	paclitaxel carboplatin	CR 40+ months	No	Lung and liver metastases	Response duration > 3x Published median (median survival 15.5 months) (108)
116	50-60, M	Metastatic castrate resistant prostate cancer	docetaxel bevacizumab thalidomide	PR 94 months	NCT 00089609	4th line; Bone metastases, pelvic adenopathy	Response duration > 3x published

							median (approximately 6 months) (109)
117	80-90, F	Soft tissue sarcoma NOS	weekly doxorubicin and concurrent radiotherapy	PR 59 months	No	Lung metastases left thigh mass	Response duration > 3x published median (4.3 months)

† 117 patients had sufficient nucleic acids for sequencing; Sequencing was unsuccessful in 6 cases; cases were grouped by tumor type; ages are grouped by decade to preserve anonymity; Abbreviations: HIPEC (Hyperthermic intraperitoneal chemotherapy); MSS (microsatellite stable); MSI (Microsatellite instability); NOS (not otherwise specified