Supplementary Figure 1. Overview of the CPIΔ cohorts. Summarising longitudinal sample collections, treatments course, sequencing, and clinical outcome data availability.

**A** ’Breast’ cohort. Metastatic TNBC cohort consisting of n=25 patients with longitudinal data available (diagram, left). Patients were randomised into 4 arms (timeline, bottom), receiving either low-dose induction therapy or no induction prior to immunotherapy, followed by CPI every 2 weeks (Nivolumab, PD-1) until progression or for a maximum of 12 months. Two biopsies were collected (timeline, top), the first (T1) prior to any treatment and second (T2) after 3-cycles of CPI. This cohort consists of NanoString RNA sequencing data and has clinical outcome data in the form of both overall survival (OS) and response defined by RECIST (table, right).

**B** “Melanoma (a)” cohort. Advanced melanoma cohort. Cohort consists of n=23 patients who were CPI naïve prior to starting the course of treatment and have longitudinal data available. All patients received CPI every 2 weeks (Pembrolizumab, PD-1), until progression, or for a maximum of 2 years. Two biopsies were collected from each patient (timeline, top), the first (T1) prior to any treatment and second (T2) after 1-cycle of CPI (23-29 days). This cohort consists of RNA-sequencing data, with clinical outcome data in the form of both overall survival (OS) and response defined by RECIST available (table, right).

**C** “Melanoma (b)” cohort. Advanced melanoma cohort. Cohort consists of n=19 patients who had previously received CPI (CTLA-4) with longitudinal data available. All patients received CPI every 2 weeks (Pembrolizumab, PD-1), until progression, or for a maximum of 2 years. Two biopsies were collected from each patient (timeline, top), the first (T1) prior to any treatment and second (T2) after 1-cycle of CPI (23-29 days). This cohort consists of RNA-sequencing data, with clinical outcome data in the form of both overall survival (OS) and response defined by RECIST available (table, right).

**D** “Pan-cancer” cohort. Metastatic solid tumor cohort consisting of n=30 patients with longitudinal data available (diagram, left) across > 5 different cancer types including, head & neck (n=3), TNBC (n=3), high-grade serous ovarian (n=6), melanoma (n=6), and a group of patients with rare solid tumors (n=12). All patients received CPI every 3 weeks (Pembrolizumab, PD-1), until progression, or for a maximum of 2 years. Two biopsies were collected from each patient (timeline, top), the first (T1) prior to any treatment and the second...
(T2) after 2 or 3 cycles of CPI. This cohort consists of RNA-sequencing data, with clinical outcome data in the form of both overall survival (OS) and response defined by RECIST (table, right).

E) “Urothelial (a)” cohort. Urothelial cohort consisting of n=64 patients with longitudinal data available (diagram, left). All patients received CPI 3 times weekly (Atezolizumab, PD-L1). Two biopsies were collected from each patient (timeline, top), the first (T1) prior to any treatment and second (T2) after all cycles of CPI. This cohort consists of RNA-sequencing data, with clinical outcome data in the form of pathological response (pCR) available (table, right).

F) “Urothelial (b)” cohort. Urothelial cohort consisting of n=13 patients with longitudinal data available (diagram, left). All patients received CPI 3 times across 42 days (ipilimumab, CTLA-4, day 1; ipilimumab + nivolumab, CTLA-4 +PD-1, day 22; ipilimumab, CTLA-4, day 42). Two biopsies were collected from each patient (timeline, top), the first (T1) prior to any treatment and second (T2) after all cycles of CPI. This cohort consists of RNA-sequencing data, with clinical outcome data in the form of pathological response (pCR) available (table, right). The illustrations in a-f were created using BioRender (https://biorender.com).

Supplementary Figure 2. Transcriptomic signature shifts in expression on-therapy across cancer-types.

A) Summary plot of all available signatures (n=32) within the ‘melanoma (a)’ cohort. Signatures are depicted on the x-axis and the proportion of patient-tumors which increase (top arrow) or decrease (bottom arrow) in expression on-therapy for each signature is indicated on the y-axis. Bars in red (OS high) and blue (OS low) depict patient stratification based on OS. Significance was tested using a Fisher’s Exact Test which is displayed.

B) Summary plot of all available signatures (n=32) within the ‘Urothelial (b)’ cohort. Bars in green (non-response) and yellow (response) depict patient stratification based on pCR.
C) Summary plot of all available signatures (n=32) within the ‘melanoma (b)’ cohort. Bars in red (OS high) and blue (OS low) depict patient stratification based on OS. Significance was tested using a Fisher's Exact Test which is displayed.

D) Summary plot of all available signatures (n=32) within the ‘Pan-cancer’ cohort. Bars in red (OS high) and blue (OS low) depict patient stratification based on OS. Significance was tested using a Fisher's Exact Test which is displayed.

E) Summary plot of all available signatures (n=28) within the ‘Urothelial (a)’ cohort. Bars in green (non-response) and yellow (response) depict patient stratification based on pCR. Significance was tested using a Fisher’s Exact Test.

Supplementary Figure 3. Genes comprising the Resistance categories across CPIΔ cohorts

A-B) Upset plots of genes comprising the a) 'Resistance Pos' and b) 'Resistance Neg' categories across the CPIΔ cohorts sub-setting for 778 genes within the NanoString Immune panel. For each upset plot, the left bar plots indicate the number of genes identified in each gene category per CPIΔ cohort, including 'breast' (pink), 'melanoma (a)' (light blue), 'melanoma (b)' (dark blue), 'urothelial (a)' (orange), 'urothelial (b)' (yellow). The top bar plot indicates the total number of genes which are unique to each cohort and the number of shared genes between cohorts, with interactions highlighted in the bottom dot plot.