Supplementary Material

Table S1 Unit cell parameter evaluation of the four 300 K data sets, with the standard deviations against the unit-cell parameters used given also.

	a (Standard deviation) **Å**	c (Standard deviation) **Å**
Unit-cell parameters (Table 1)	79.86	37.80
Data set 1	79.62 (0.16)	37.73 (0.04)
Data set 2	79.90 (0.02)	37.78 (0.01)
Data set 3	79.69 (0.12)	37.68 (0.08)
Data set 4	79.25 (0.43)	37.58 (0.15)

Taking into account the standard deviations between the unit cell parameters used in processing the data and the unit-cell parameters of each run using the first 20 images, each are within 2 sigma except for data set 4. Due to this change in data set 4, data set 4 was re-integrated and reprocessed using the unit-cell parameters of the first 20 images. However, after re-integration and re-processing the unit-cell parameters did not differ greatly, as compared with the original unit-cell parameters used (a = 79.87, c = 37.76 versus other Table 1 values). Hence between the first data set and the fourth data set the 'a' unit-cell parameter was very similar, thus the unit-cell parameters used for data sets 2 and 3 must also have been very similar, so that no significant increase in the unit cell was seen at these high radiation doses. The intrinsic variations seen suggest that the quoting of the sigmas to 2 decimal places by the software is over optimistic but are given here for completeness.

Table S2. The Pt-N distances in Å are given along with the precisions of these bonds in parantheses based on the Cruickshank DPI coordinates (see Table 1) for each pair of atoms (Pt and N) for each model refinement to give an indication specific to these atoms of the precision of their separation ie with their individual B factors taken into account

	Pt to N distance in Nδ binding site	Pt to N distance in Nε binding site
100K data collection	2.1Å (0.3)	2.2Å (0.3)
300K data collection. Data set 1	2.3Å (0.4)	2.4Å (0.4)
300K data collection. Data set 2	2.6Å (0.5)	2.6Å (0.5)
300K data collection. Data set 3	2.3Å (0.7)	2.4Å (0.8)
300K data collection. Data set 4	2.4Å (0.8)	2.2Å (0.7)

Note: These Pt to histidine nitrogen distances are unrestrained values from the refinement. The nitrogen atoms within the imidazole ring itself are of course restrained.

Table S3

	300 K crystal X-ray dose estimation.

Chemical Formula used taken into account the solvent contents	$C_{611.01}\,N_{192.01}\,O_{523.01}\,S_{11.0003}\,Na_{10}\,Cl_{10.014}\,Pt_{1.27}$ *
X-ray Intensity (photons/sec/mm^2)	$5x10^9$ **
Total exposure time (sec)	Runs 1 and 2 = 28800 Runs 3 and 4 = 43200
Sample size (mm)	0.15 0.15 0.10
Sample cross sectional area presented to the incident X-ray beam (mm^2)	$0.025mm^2$
Sample volume (cm^3)	(0.015 x0.015 x 0.01) $cm^3 = 2.25x10^{-6}\,cm^3$
X-ray beam fraction absorbed	$1\text{-}e^{-\mu d}$ (μ =1.51 mm^{-1}, d= 0.1 mm) = 0.14 (14%) [a]
Photon energy (eV)	8042
Conversion factor 1 eV to 1 Joule	$1.6x10^{-19}$ J
Crystal mass (g) = (density (g/cm^3) x volume (cm^3))	0.810 g/cm^3 x $2.25x10^{-6}\,cm^3 = 1.82x10^{-6}$ g
Absorbed X-ray dose (J/g); (a) data sets 1 and 2 (b) datasets 3 and 4	(a) $5x10^9$ x 0.025 x $2.88x10^4$ x 0.14 x 8042 x $1.6x10^{-19}$ / $1.82x10^{-6}$ = 356.32 J/g = 0.36 MGy (b) $5x10^9$ x 0.025 x $4.32x10^4$ x 0.14 x 8042 x $1.6x10^{-19}$ / $1.82x10^{-6}$ = 534.48 J/g = 0.53 MGy
Individual dataset X-ray	Run 1 = 0.36 MGy

absorbed doses	Run 2 = 0.36 MGy Run 3 = 0.53 MGy Run 4 = 0.53 MGy
Total X-ray absorbed Dose	1.78 MGy
	Allowing for errors and inaccurate estimates this sample has absorbed ~1.8MGy

Absorbed dose = Intensity x exposure time x sample cross sectional area x beam absorbed fraction x photon energy x $1.6x10^{-19}$ / Crystal mass

The calculation used to obtain the numbers of waters, NaCl ion pairs, DMSO and cisplatin/carboplatin molecules in the solvent portion of the space group's asymmetric unit was:-

Solvent content fraction x unit cell volume (in $Å^3$) x 0.125 ($1/8^{th}$ of the unit cell volume ie the volume of the asymmetric unit in the space group $P4_32_12$) x 10^{-24} cm^3 (to convert the unit cell volume from $Å^3$ to cm^3) x Avogadro's Number x concentration (in Moles) / 1000 (in cm^3 ie the volume for 1 M).

* The chemical formula for the ordered portion of the asymmetric unit is $C_{609}N_{192}O_{187}S_{11}Pt_{1.2}$

And the chemical formula for the solvent channel derived from the above formula is $C_{2.01}N_{0.01}O_{336.01}S_{0.0003}Na_{10}Cl_{10.014}Pt_{0.07}$

**** The incident X-ray intensity estimate is approximately what a modern sealed tube microfocus X-ray source with suitable modern X-ray beam conditioning optics can deliver.

a The linear absorption coefficient was calculated using SHELX for the chemical formula sum of the ordered portion of the unit cell asymmetric unit and the solvent fraction of the asymmetric unit.

The above evaluation and conditions can be compared with those used in cancer patient combination therapy. For curative cancer cases, the typical dose for a solid epithelial tumor ranges from 60 to 80 Gray (Gy), while lymphomas are treated with 20 to 40 Gy. Preventative (adjuvant) doses are typically around 45 – 60 Gy in 1.8 – 2 Gy fractions (for breast, head, and neck cancers.). The photon energy used in radiation therapy is in the voltage range of 4-25 MeV as these penetrate well to deep sites within the body.

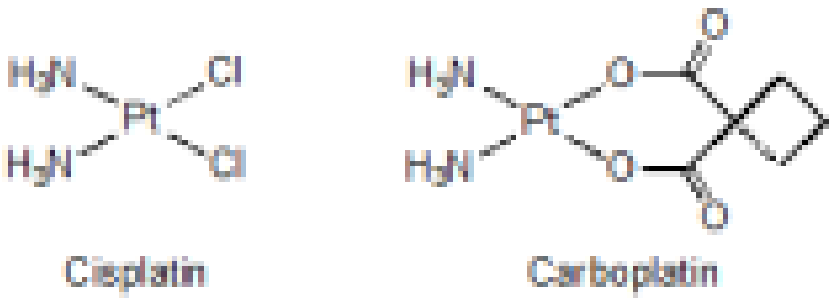

Figure S1. Chemical structures of cisplatin and carboplatin.

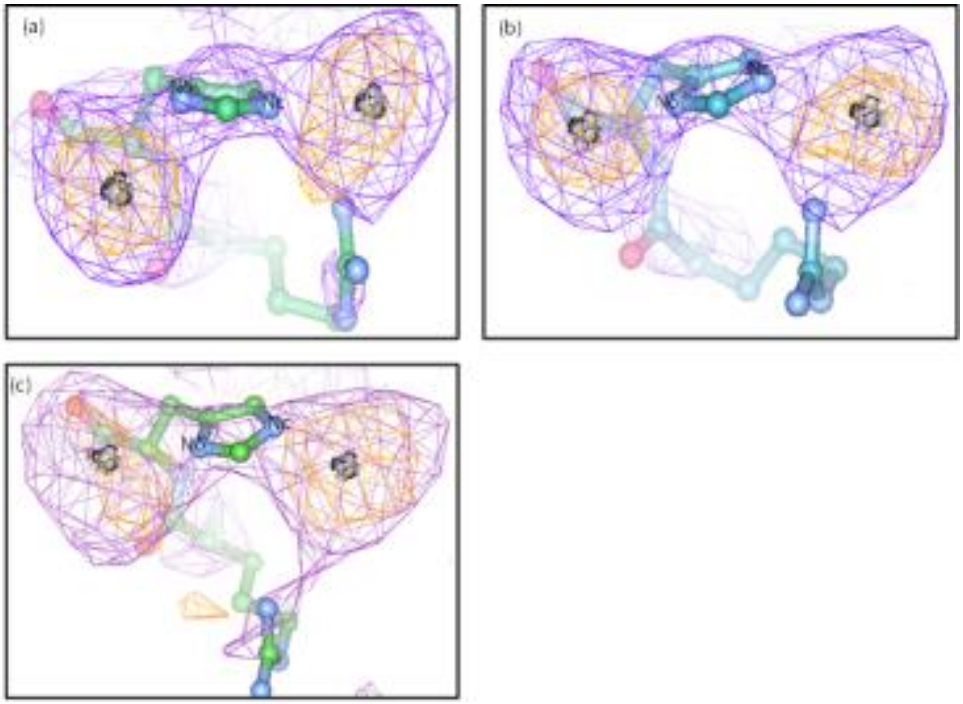

Figure S2. Cisplatin binding to His15 of HEWL at RT after continued X-ray irradiation. (a) RT data set 2, (b) RT data set 3, (c) RT data set 4. The 2Fo-Fc map (in purple) is at the 1.5 rms cutoff level and the anomalous difference density map (in orange) is at the 3σ cutoff level. The Nδ and Nε atoms in the imidazole ring are labelled along with the Pt, N and Cl atoms of the bound cisplatin moiety. [These detailed atom assignments are based on the 100 K and 300 K data set 1; for details see main text.]

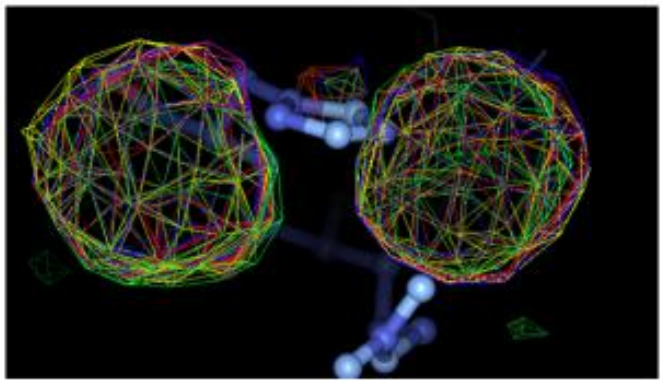

Figure S3. The difference electron-density OMIT maps for the four 300 K X-ray data collection runs after rigid-body protein-model refinement with all cases having their diffraction data cut at 3.5 Å resolution. Green is data set 1, blue data set 2, red data set 3 and yellow data set 4.

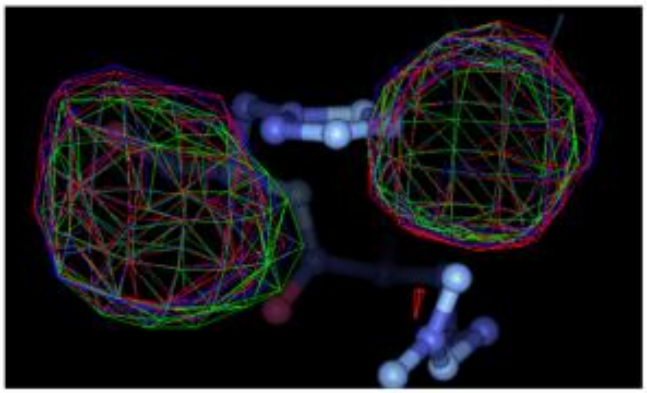

Figure S4. The difference electron-density OMIT maps for the first three data sets at 300 K data collection after rigid-body protein-model refinement all cut at 2.9 resolution. Green is data set 1, blue data set 2 and red data set 3.