CANCER RESEARCH HORIZONS

Best-in-class Phase I DNA-dependent protein kinase (DNA-PK) inhibitor: AZD7648

Tech ID: CR1997-016
CRH Deck 2025

FURTHER FASTER TOGETHER
We are beating cancer

Quick Factsheets

CANCER RESEARCH HORIZONS

Small molecule series

AZD7648; AZD-7648; DNA-dependent protein kinase (DNA-PK) inhibitor

AZD7648 is a potent and highly selective DNA-PK inhibitor *(cellular potency IC_{50} value = 91.3 nM, NSCLC cell line; A549).*

USPs: Selectivity & Differentiated NHEJ MoA

AZD7648 exhibits minimal off-target effects with superior selectivity for DNA-PK versus closely related kinases; PI3K, ATM, ATR & mTOR.

Mechanisms of action (MoA): AZD7648 disrupts Non-Homologous End Joining (NHEJ) repair of double-stranded breaks (DSB). AZD7648 blocks DNA-PK autophosphorylation and activity, leading to genome instability and apoptosis.

Substantive preclinical data

- ✓ Upregulation of DNA-PK is associated with poor prognosis and decreased response to DNA-damaging agents across cancer types.
- ✓ AZD7648 synergises with standard of care treatments that increase DSB incidence; sensitising cancers to ionising radiation (IR), topoisomerase II (doxorubicin) and PARP inhibitors.
- ✓ AZD7648 single agent and combinations induced tumour regression in non-small cell lung, breast (TNBC), ovarian, and head and neck cancer xenografts including some ATM-deficient, BRAC1 and TP53 mutants PDX.
- ✓ AZD7648 and targeted IR promotes improved tumour control and immunologic memory against tumour antigens.

Phase I

Highest stage of development: Phase I

NCT03907969: Phase I/IIa study initially planned to investigate AZD7648 monotherapy, or in combination with pegylated liposomal doxorubicin "PLD") in participants with advanced cancers. Last patient enrolled 2022.

Intellectual property

WO2018114999A1 (lead series) and WO2019238929 (second series).

Composition of matter patents filed in 2019, by AstraZeneca and CRH, covering amino-triazolopyridine or purinone compounds and their use in treating cancer. Worldwide applications incl. US, EU, CN, JP, AU, CA, KR, BR

>$8.93Bn* 2025

The Global DNA Damage Repair Drugs Market is on a high-growth trajectory. The median market size is estimated at $8.93 billion (USD) in 2025 and projected to reach ~$16.25 billion by 2030, CAGR of 14%.

Seeking

Co-development and licensing partners interested in advancing the clinical development of AZD7648 in oncology. Specifically, the use of AZD7648 in combination with DSB-inducing agents (incl., Top II inhibitors or next gen ADCs, RTx , PARP inhibitors). We also welcome collaborations in CRISPR genome editing.

Figure 1. DNA-PK is a Multifaceted Player in DNA Damage & Replication Stress Responses

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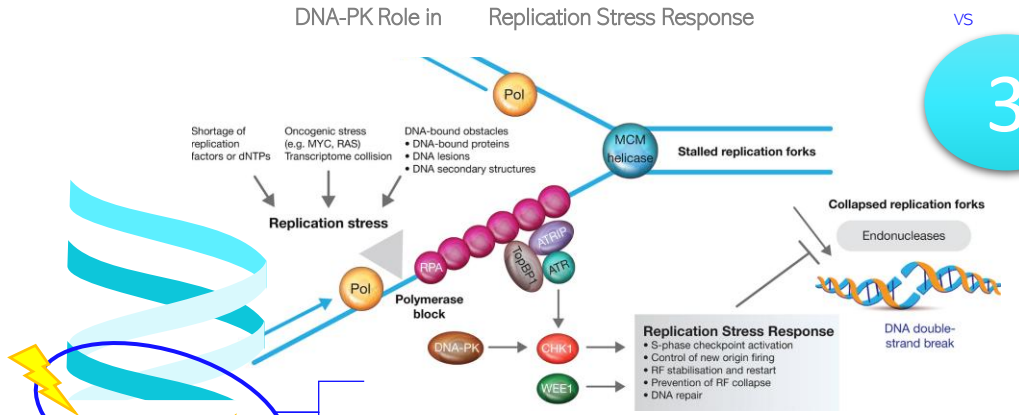
1

Double-strand breaks (DSB); DSBs are considered the most deleterious of DNA lesions. Generated endogenously (i.e., RO species, recombination) or exogenously by ionising radiation (IR), DSB-inducing therapies (bleomycin, Topo II; doxorubicin & etopsides etc)



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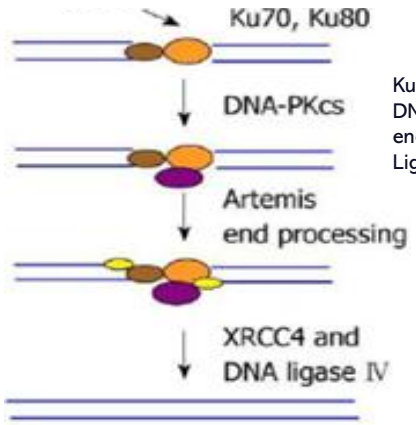


Ku70/80 recognises DSB; recruits DNA-PK for repair; Artemis facilitates endonuclease activity; XRCC4/DNA Ligase IV ligate DNA ends.

Single-strand break (SSB);

PARP inhibitors trap PARP onto DNA at SSBs; which in turn stalls replication forks and generates DSBs.

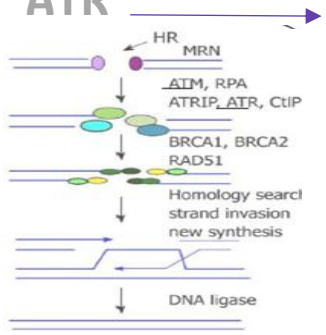
Repair targets

DNA-PK

2

ATM

ATR



Repair Pathways

Non-Homologous End Joining (NHEJ)

- Fast DSB repair (minutes to hours).
- Does not require homologous template.
- Any cell cycle phase (ideally early G1/S).

Combination Partners:

- RTx
- Topoisomerase II inhibitors

Homologous Recombination Repair (HRR)

- Slower DSB repair (hours to days).
- Requires homologous template.
- Only active in S & G2 phase.

Combination Partners:

- RTx
- Topoisomerase I inhibitors
- Nucelotise analougue

DNA-dependent protein kinase (DNA-PK), Ataxia Telangiectasia Mutated (ATM), Ataxia Telangiectasia and Rad3-related protein (ATR),

- DNA-PK is the master regulator of canonical NHEJ, which repairs most DSBs in human cells. Repair of DNA DSB generated by IR and topo II inhibitors mainly requires DNA-PK, lending rationale to combining DNA-PK inhibition alongside these agents.
- In ATM-deficient cancers, DNA-PK inhibition may heighten genomic instability, leading to growth arrest and apoptosis

Untapped therapeutic potential of targeting DNA-PK in cancers.

DNA-PK has diverse cellular functions and influences cancer progression, making its distinct activities attractive selective targets for innovative cancer therapeutics.

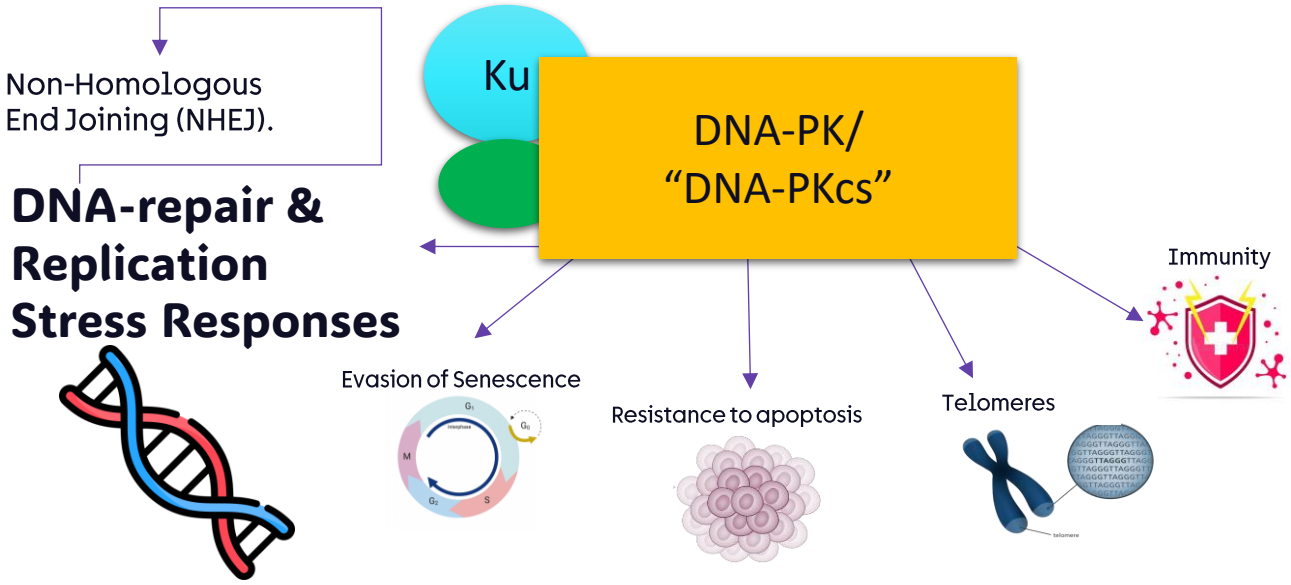


Figure 2. Exemplar pleiotropic impacts of DNA-PK;

- DNA-PK is vital for efficient NHEJ / DSB DNA repair. Contributes to DNA fork stabilisation and repair under replication stress.
- Aids the recruitment of essential DDR repair proteins.
- DNA-PK phosphorylates p53 (apoptosis) and impacts PCD induction.
- DNA-PK is involved in telomere capping and length maintenance.
- DNA-PK plays a role in V(D)J recombination and immuno-globulin class switch recombination for T and B-cell development.

Technical Background:

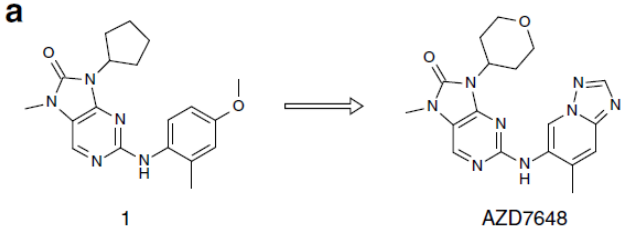
- **DNA-dependent protein kinase (DNA-PK; DNA-PKcs)** is a nuclear serine/threonine protein kinase and member of the phosphatidylinositol 3-kinase-related kinase (PI3K) superfamily alongside ATM and ATR.
- A key player in **DNA damage response (DDR)** and repair processes; activated DNA-PK orchestrates rapid, template-independent repair of DNA **double-strand breaks (DSBs)** via the **non-homologous end joining (NHEJ)** pathway, while also responding to replication stress.
- The pleiotropic impacts of DNA-PK transforms the paradigm and utility of targeted DNA-PK inhibitor therapy in cancer treatment. **- Figure 2**
- Cumulative evidence highlights DNA-PK overexpression and hyperactivation acts as an oncogenic driver in advanced cancers influencing cell cycle progression, tumour metastasis, metabolic regulation and immunity.
- DNA-PK aids tumour cell inherent genomic instability via DDR processes and also affords protection from therapy induced DSBs. DNA-PK inhibition has potential in combination with DSB-inducing therapies, RTx and TopII inhibitors, to achieve deeper clinical responses.

AZD7648: Potent and selective DNA-PK inhibitor developed as an oral antitumour agent

Mechanistic validation and *in-vitro* cellular pharmacology

Figure 3. AZD7648 Molecular Diagram (3A). (3B) Western blot analysis of markers in cells exposed to increasing AZD7648 concentrations and 1h pre-treatment of ± 8 Gy IR . (3C) Cellular Pharmacology of AZD7648.

a



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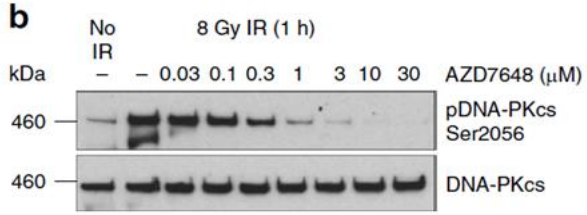

c

Assay target	IC_{50}, *n* (pIC_{50} ± 2 SEM)
DNA-PKcs	91.3 nM, 13 (7.04 ± 0.15)
ATM	17.93 μM, 7 (4.75 ± 0.15)
ATR	>29.77 μM, 5 (<4.53 ± 0.005)
PI3Kα	>8.03 μM, 6 (5.07 ± 0.2)
PI3Kβ	>30 μM, 5 (<4.53)
PI3Kγ	1.37 μM, 7 (5.86 ± 0.35)
PI3Kδ	>30 μM, 7 (<4.53)
mTOR	>30 μM, 4 (<4.53)

Results are presented as geometric mean IC_{50} and number of repeats, *n*. The mean pIC_{50} ± 2 SEM are described in parentheses. pIC_{50}, –log (IC_{50})

IC_{50} = concertation giving 50% of the drug-induced inhibitory effect.

Fok et al., 2019

Figure 3a Resultant Screening Hit "1" exhibited good selectivity for DNA-PK versus PI13Kα; further optimisation to increase potency, improve physicochemical properties and pharmacokinetics led to the novel molecular entity: AZD7648

- AZD7648 is achiral and has a relative molecular mass of 380.40.

AZD7648 limits DNA-PKcs autophosphorylation at Ser2056 (Figure 3b)

- In IR-treated A549 cells (NSCLC line), AZD7648 potently inhibits DNA-PKcs autophosphorylation at Ser2056. pSer2056, pRPA32 and γH2AX at Ser4/Ser8 were key DNA-PK PD markers modulated by AZD7648 in a dose dependent manner.
- DNA-PK catalytic subunit autophosphorylation site at Ser2056 is important for modulating the conformational state necessary for DNA end processing and ligation during NHEJ repair.

AZD7648 is a potent nanomolar inhibitor of DNA-PK kinase activity with IC50 values of 0.63 nM and 91.3 nM for isolated enzyme and cellular potency, respectively.

AZD7648 exhibited >90-fold cellular selectivity over ATM, ATR, mTOR, and three PI3K isoforms (PI3Kα, PI3Kβ and PI3Kδ) and >10-fold selectivity over PI3Kγ

- Competitive data: 1st and 2nd Gen DNA-PK inhibitors; KU-0060648, NU7441 and M3814 all exhibited <10-fold selectivity in at least one secondary pharmacology target (e.g., ATM, mTOR, PI3K).

AZD7648 is an impressive chemo- and radiosensitiser

Pre-clinical data highlights AZD7648 induces tumour regressions when combined with RTx, TopII and PARP Inhibitors

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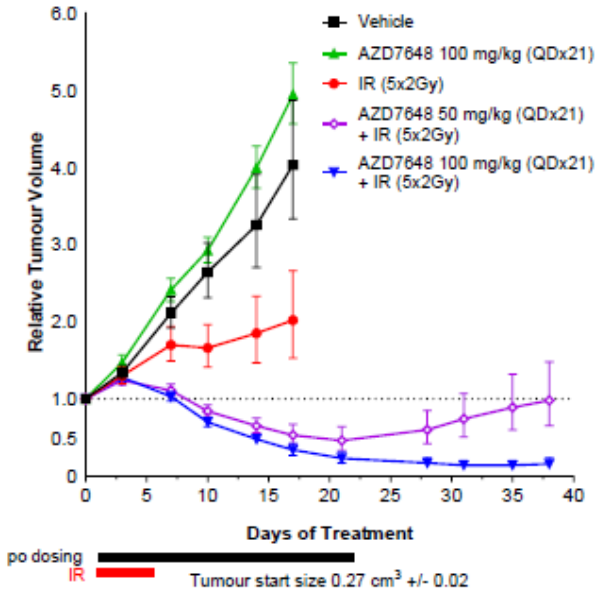
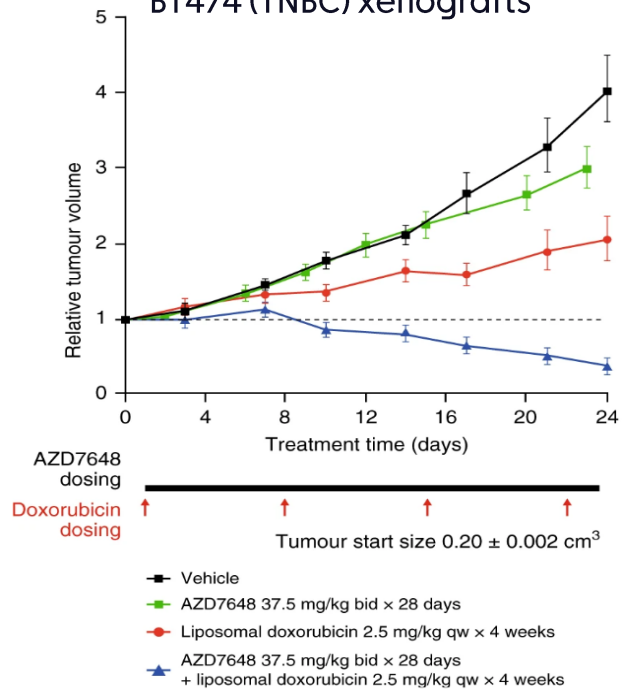
Ionising Radiation (IR) & DNA-PKi (AZD7648)

Figure 4. AZD7648 induces tumour regression in combination with IR in NCI-H1299 (NSCLC) xenografts



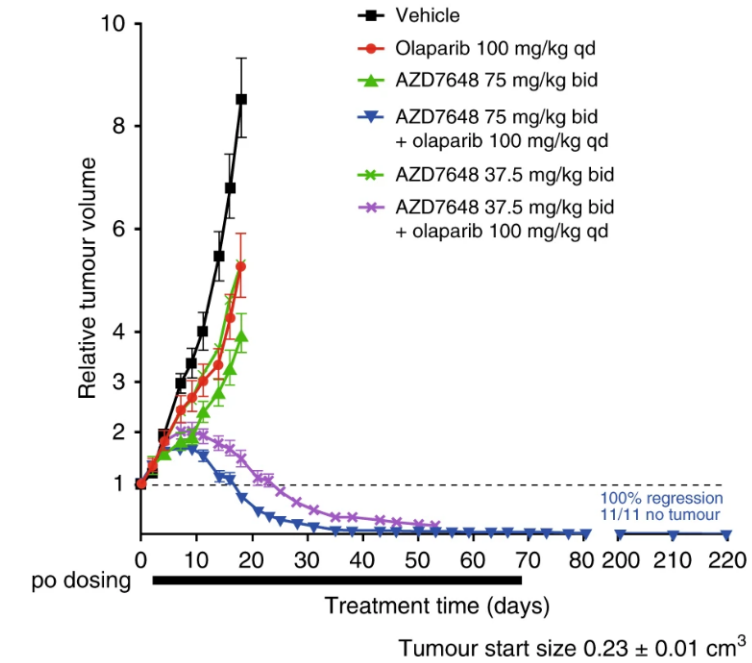
Topo II inhibitor & DNA-PKi (AZD7648)

Figure 5. AZD7548 induces tumour regression in combination with liposomal doxorubicin in BT474 (TNBC) xenografts



PARP & DNA-PKi (AZD7648)

Figure 6. AZD7648 induces complete tumour regression in combination with olaparib in FaDu ATM KO (Head & Neck) xenografts



- Across *in-vivo* models AZD7648 in combination with ionising radiation led to significant tumour volume regression *(e.g., in NCI-H1299-NSCLC 85% TGI achieved for combo: AZD7648, 100mg kg-1 + IR vs 60% TGI IR alone)* **– Figure 4 (Fok et al., 2019).**
- Radiotherapy and AZD7648 treatment leads to durable immune-mediated tumour control. Blocking type I IFN was critical for tumour growth control following combined therapy **– Nakamura et al., 2021.**
- AZD7648 significantly increased the efficacy of liposomal doxorubicin and resulted in tumour regression across solid tumours including TNBC *in-vivo* models *(e.g., in BT474 AZD7648 caused 20% TGI, doxorubicin alone 63%, combo 77% regression)* **– Figure 5 (Fok et al., 2019).**
- AZD7648 induces complete tumour regression in combination with olaparib in mice implanted with FaDU ATM KO xenografts **– Figure 6 (Fok et al., 2019)**. Non-clinical data packages demonstrates AZD7648 and PARPi combination may have potential benefit in genetic background beyond ATM-deficiency; TP53 and BRCA1/2 mutants, among others.

Tech ID:CR1997-016; September 2025

AZD7648 positively differentiates from its key competitors based on selectivity and on target coverage at achievable clinical exposure.

Table 1. Summary of AZD7648 Profile

		AZD7648	M3814
Cellular on- vs off- target kinase IC50 [μM)]	DNA-PK	0.09	0.04
	ATM/ATR	18/>30	>30/>30
	PI3K α/β/γ/δ	>8/>30/1.4/>30	0.8/0.17/0.16/0.35
	mTOR	>30	0.55
Clinical PK	Free $AUC_{(0-12)}$	20.6 μM.h at 160mg BID	• BJC (2021) 124:728–735; • Journal of Clinical Oncology36, no.36, no.15_suppl (May 20, 2018) 251815_suppl (May 20, 2018) 2518-2518.
	Free Cmax	3.6 μM.h at 160mg BID	
Target Coverage @ highest mono dose Cmax	DNA-PK	At 160 mg, achieves IC_{50} coverage > 24hrs, IC_{90} ~15hrs	
	PI3Kα/β, mTOR IC_{50}	> 3- 10x window from off-target IC_{50}	
Clinical Trial Design, Safety & Tolerability NCT03907969; AZD7648 monotherapy and PLD combination. *- Yap et al., 2025*	Modular Phase I/IIa, open-label, multicentre study in advanced cancers. • Core Monotherapy Module (AZD7648) vs Combination module 1 (AZD7648 + Pegylated liposomal doxorubicin "PLD") • Monotherapy doses ranged between 5mg to 160mg BID (n = 14) vs combination ranging between 5 to 20 mg QD for AZD7648, with PLD 40 mg/m^2 (n = 16) • Between 2019 to 2022, ~30 patients (>18yrs) with advanced malignancies (e.g., lung, liver, ovary, endometrial pancreas among others) were enrolled in dose-escalation cohorts (module 1 and 2) ; Monotherapy – Module 1 • Mean treatment length (2.9 months); frequent class of adverse events were gastrointestinal disorders (9/14 patients, 64.3%); 1/14 DLT (patient at 160 mg BID). Combination – Module 2- AZD7648 + PLD • Mean treatment length (3.42 months); maximum dose of combination therapy was AZD7648 40 mg QD days 1–7 + PLD every 28 days. 13/16 patients (81.3%) experienced gastrointestinal disorders, and 11/16 (68.8%) patients had anaemia. 3/16 DLTs at 20-30mg QD 7 days + PLD. • One RECIST partial response observed for AZD7648 plus PLD combo in a cervical adenocarcinoma patient putatively with ATM deficiency, MMR mutations "MLH1" or MSI-H phenotypes. *Clinical data available under CDA.*	

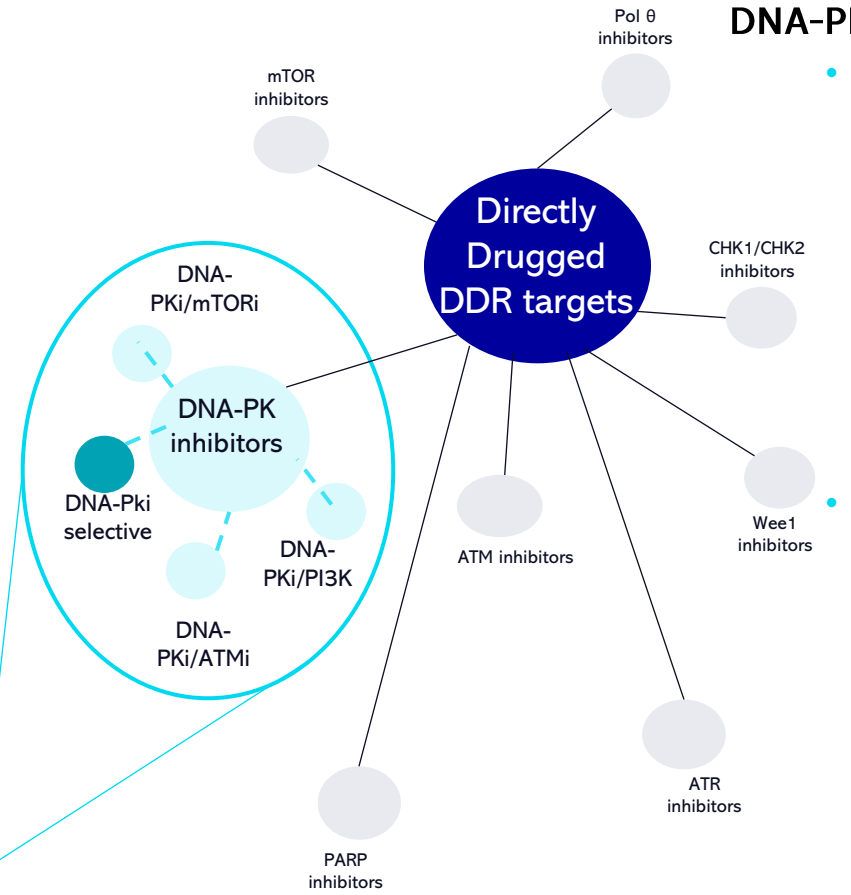
Competitive landscape:

DNA-PK inhibitors are emerging as a key growth segment in the evolving DNA Damage Response market

Table 2. Small molecule DNA-Pk inhibitor pipeline

Drug	Stage of Development			Indications & Clinical Strategy
	Pre-clinical	Phase I	Phase II	
AZD7648*			**	Phase I complete. Trial investigated AZD7648 monotherapy and combination with PLD in advanced malignancies including NSCLC, ovarian, and TNBC. NCT03907969
CC-115			***	Dual DNA-PK/mTOR inhibitor; Phase I/II studies in GBM, prostate, CLL; combos with radiotherapy and chemotherapy; *NCT01353625, NCT02833883*
SF-1126				Pan-PI3K inhibitor
M3814* (peposertib)			**	Explored in advanced solid tumours and leukaemia. Combination with chemoradiotherapy, Etoposide/cisplatin, Radiotherapy. *NCT02316197, NCT03116971, NCT02316197*
XRD-0394				DNA-ATM dual inhibitors. Ongoing early clinical investigation for metastatic, locally advanced solid tumours or recurrent cancers; *NCT05424097*
Bosmolisib (BR-101801)			***	Triple inhibitor of PI3K γ/δ and DNA-PK. Phase I/II in B and T-cell Lymphoma. NCT04018248.

(* dark turquoise) = selective DNA-PK inhibitors
(** - grey) = Planned phase II not conducted.
(*** light blue) = Phase II (not yet recruiting / recruiting / ongoing).



AZD7648 advantages compared to competing DNA-PK inhibitors (DNA-Pki):

- AZD7648 is a highly potent and selective DNA-PK with >90-fold selectivity over related kinases, minimising off-target effects.
  - Competing small molecule DNA-Pki, CC-115 and Bosmolisib, are in Phase I/II clinical trials but, unlike AZD7648 and M3814, they are known to be multi-kinase inhibitors (mTOR, PI3K, ATM).
- Compared to M3814, AZD7648 combined with radiotherapy leads to more durable and effective tumour suppression in diverse cancer pre-clinical models.
  - AZD7648 shows potent synergy with ionising radiation leading to complete regression or profound tumour regression (>75%) in adenocarcinoma (MC38), colorectal (CT26), and melanoma (B16-F10) models, with CD8+ T-cell and IFN-dependent durable tumour control.

Seeking co-development and licensing partners

Future Development Plans

We are seeking partners to advance AZD7648 clinical development by optimising its therapeutic potential in defined cancer populations, exploring strategic combination approaches, and/or extending its application to innovative medical technologies such as CRISPR genome editing.

Clinical Development Scope: Oncology

AZD7648 clinical results highlight promising directions for continued exploration and development. Optimised strategies to enhance the therapeutic index to maximise efficacy and minimise toxicity in multiple cancers could include;

- Combinations with localised RTx (IR to stereotactic RTx), topoisomerase II inhibitors (including next-generation ADCs), or PARP inhibitors. Tumour-targeting chemo/radiotherapy approaches such as radioimmunoconjugates could be explored.
- Incorporating precise biomarker-guided dose scheduling and prophylactic use of G-CSF or anti-emetic drugs to overcome on-target toxicities.
- Further investigation into relevant genetic backgrounds conferring sensitivity to DNA-Pk inhibitors (e.g., ATM or TP53 loss-of-function mutations, MMR mutations “MLH” or “MSI-H “phenotypes).

Auxiliary technology and medical applications

- Data exemplifies AZD7648 enhances homology-directed repair (HDR) efficiency, which could be leveraged to increase the precision and scale of alterations achievable with novel HDR-driven CRISPR-Cas9 genome editing technologies.- *Cullot et al., 2024.*

Technology Summary

DNA-PK is a core component of the DNA Damage Response and orchestrates the repair of both spontaneous and therapy induced double-strand breaks (DSBs) via the non-homologous end joining (NHEJ) pathway. Developed by AstraZeneca & Cancer Research Horizons, AZD7648 is a clinical-stage highly potent and selective small molecule DNA-PK inhibitor with favourable PK/PD properties and on-target coverage at achievable clinical exposure. By impeding NHEJ-directed DSB repair, amplifying genomic instability and driving apoptosis in cancer cells, AZD7648 demonstrates a differentiated mechanism of action with best-in-class potential.

AZD7648 exhibits minimal off-target activity across structurally related kinases (PI3Kα/δ, ATM, ATR, mTOR), surpassing competing DNA-PK inhibitors in selectivity. While moderate monotherapy efficacy was observed in some ATM-deficient cell lines and xenografts, AZD7648 strength lies in its broad applicability as a combination partner. Preclinical studies in solid tumour models highlight AZD7648 treatment enhanced sensitivity to ionising radiation, topoisomerase II inhibitors (e.g., doxorubicin), and synergies with PARP inhibition in ATM-deficient PDX models.

In 2019, an open-label Phase I/IIa trial launched to evaluate AZD7648 in advanced malignancies as a single agent and in combination with pegylated liposomal doxorubicin (PLD). Phase I results indicate limited efficacy, and GI toxicities were the most common adverse event in patients, reflecting some of the on-target toxicities exhibited by competing DNA-PK inhibitors (i.e., M3814 - peposertib). Nevertheless, AZD7648 could be effectively optimised for use in combination with localised RTx (IR to stereotactic radiotherapy), topoisomerase II (incl. next-gen ADCs) and PARP inhibitors; and may have potential alongside tumour-targeting chemo/radiotherapy (incl. radioimmunoconjugates). Combinatorial approaches may be particularly promising in cancer patients characterised by ATM deficiency.

Substantive pre-clinical and clinical data

Key publications supporting medical applications of AZD7648

CANCER RESEARCH HORIZONS

Article | Open access | Published: 07 November 2019

AZD7648 is a potent and selective DNA-PK inhibitor that enhances radiation, chemotherapy and olaparib activity

Jacqueline H. L. Fok, Antonio Ramos-Montoya, Mercedes Vazquez-Chantada, Paul W. G. Wijnhoven, Valeria Follia, Neil James, Paul M. Farrington, Ankur Karmokar, Sophie E. Willis, Jonathan Cairns, Jenni Nikkilä, David Beattie, Gillian M. Lamont, M. Raymond V. Finlay, Joanne Wilson, Aaron Smith, Lenka Oplustil O'Connor, Stephanie Ling, Stephen E. Fawell, Mark J. O'Connor, Simon J. Hollingsworth, Emma Dean, Frederick W. Goldberg, Barry R. Davies & Elaine B. Cadogan

Nature Communications **10**, Article number: 5065 (2019) | Cite this article

Scan or click for the Fok et al., 2019 publication.

Article | Open access | Published: 17 May 2025

Clinical Studies

The DNA-PK inhibitor AZD7648 alone or combined with pegylated liposomal doxorubicin in patients with advanced cancer: results of a first-in-human Phase I/IIa study

Timothy A. Yap, Patricia LoRusso, Rowan E. Miller, Rebecca Kristeleit, Amanda G. Paulovich, Stephen McMorn, Lenka Oplustil O'Connor, Benedetta Lombardi, Paola Marco-Casanova, Eric T. Gangl, Bharat Patel, Mark J. O'Connor, Emma Dean, Roman Zviezdin & Ruth Plummer

British Journal of Cancer **133**, 168–177 (2025) | Cite this article

Scan or click for the Yap et al., 2025 publication.

TRANSLATIONAL CANCER MECHANISMS AND THERAPY | AUGUST 01 2021

Inhibition of DNA-PK with AZD7648 Sensitizes Tumor Cells to Radiotherapy and Induces Type I IFN-Dependent Durable Tumor Control

Kyoko Nakamura; Ankur Karmokar; Paul M. Farrington; Neil H. James; Antonio Ramos-Montoya; Susan J. Bickerton; Gareth D. Hughes; Timothy M. Illidge; Elaine B. Cadogan; Barry R. Davies; Simon J. Dovedi; Viia Valge-Archer

Check for updates

+ Author & Article Information

Clin Cancer Res (2021) 27 (15): 4353–4366.

https://doi.org/10.1158/1078-0432.CCR-20-3701 **Article history**

Scan or click for the Nakamura et al., 2021 publication.

Brief Communication | Open access | Published: 27 November 2024

Genome editing with the HDR-enhancing DNA-PKcs inhibitor AZD7648 causes large-scale genomic alterations

Grégoire Cullot, Eric J. Aird, Moritz F. Schlapansky, Charles D. Yeh, Lilly van de Venn, Iryna Vykhlyantseva, Susanne Kreutzer, Dominic Mailänder, Bohdan Lewków, Julia Klermund, Christian Montellese, Martina Biserni, Florian Aeschimann, Cédric Vonarburg, Helmuth Gehart, Toni Cathomen & Jacob E. Corn

Nature Biotechnology (2024) | Cite this article

Scan or click for the Cullot et al., 2024 publication.

Phase 1 Best in class DNA-PK inhibitor

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FURTHER FASTER TOGETHER
We are beating cancer

TechID: CR/1997-016

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FURTHER FASTER TOGETHER

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Best in class phase 1 DNA-PK inhibitor

Best-in-class phase 1 small molecule DNA-dependent protein kinase (DNA-PK) inhibitor which positively differentiates from its key competitors based on selectivity and on target coverage at achievable clinical exposure.

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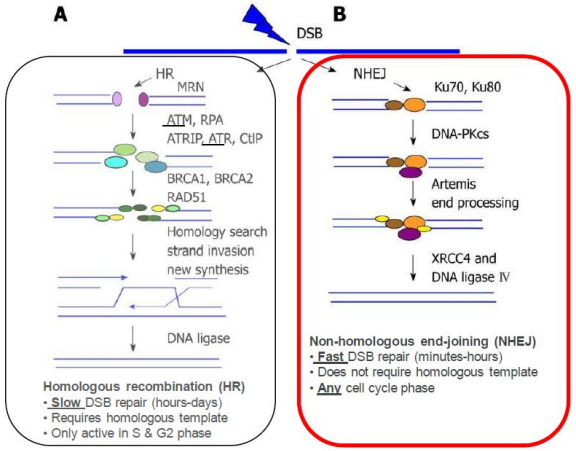

Figure 1. DNA -PK is a crucial component of the Non-Homologous End Joining (NHEJ) repair pathway and represents an opportunity for a differentiated mechanism of action.

Cellular on- vs off- target kinase IC_{50} [μM]	DNA-PK	0.09
	ATM/ATR	18/>30
	PI3Kα/β/γ/δ	>8/>30/1.4/>30
	mTOR	>30
Clinical PK	Free $AUC_{(0-12)}$	20.6 μM.h at 160mg BID
	Free Cmax	3.6 μM.h at 160mg BID
Target Coverage @ highest mono dose Cmax	DNA-PK	• At 160 mg, achieves IC_{50} coverage > 24 hrs, IC_{90} coverage ~ 15 hrs
	PI3Kα/β, mTOR IC_{50}	• > 3-10x window from off-target IC_{50}

Figure 2. AZD7648 positively differentiates from its key competitors based on selectivity and on target coverage at achievable clinical exposure.

Mechanism and key data summary

DNA-dependent protein kinase (DNA-PK) is involved in DNA damage response (DDR) and activated in response to DNA double stand breaks (DSB) induced by radiation and topoisomerase II inhibitors. DNA -PK is a crucial component of the Non-Homologous End Joining (NHEJ) repair pathway and represents an opportunity for a differentiated mechanism of action.

AZD7648 is a potent and highly selective DNA-PK inhibitor well tolerated as monotherapy within predicted dose range in a phase 1 trial.

AZD7648 is shown to be an efficient sensitizer of radiation- and doxorubicin-induced DNA damage, with combinations in xenograft and patient-derived xenograft (PDX) models inducing sustained regressions.

Immuno-proficient xenograft models have a superior response to radiation in combination with AZD7648 than immuno-deficient models, suggesting an immune component to response.

AZD7648 enhances PARP inhibitor olaparib's efficacy across a range of doses and schedules in xenograft and PDX models, enabling sustained tumour regression and providing a clear rationale for its clinical investigation.

Translation and commercialisation

- Through its differentiated mechanism of action as an NHEJ inhibitor, AZD7648 has potential in combination with DDR-targeted agents to achieve deeper responses to current therapies.
- Composition of matter patent WO 2018/114999 granted in extended worldwide territories
- Seeking collaboration and licensing opportunities

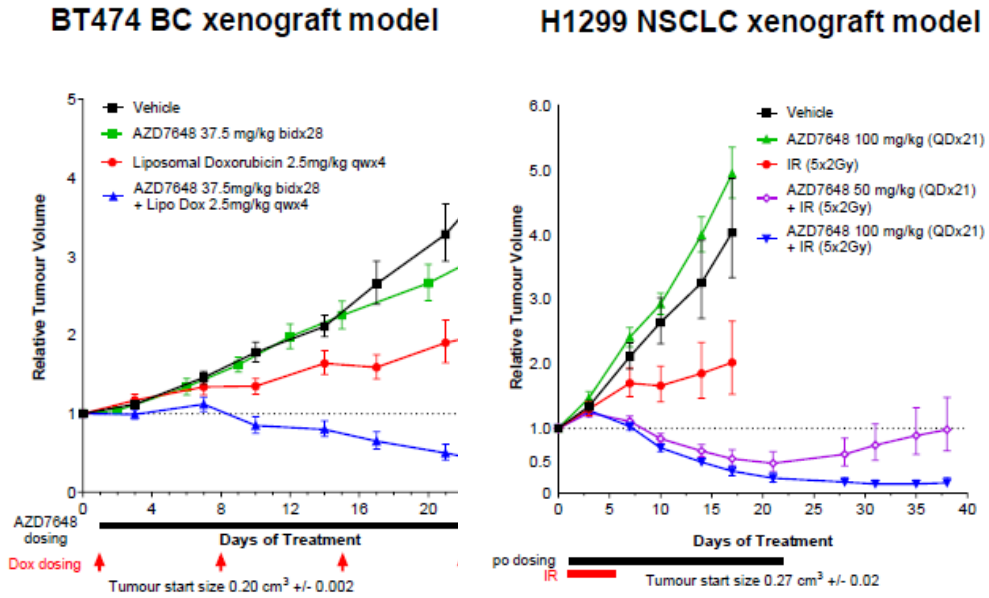

Figure 3. AZD7648 is shown to be an efficient sensitizer of radiation- and doxorubicin-induced DNA damage, with combinations in xenograft and patient-derived xenograft (PDX) models inducing sustained regressions.

Publications

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1. Fok, J.H.L., Ramos-Montoya, A., Vazquez-Chantada, M. et al. AZD7648 is a potent and selective DNA-PK inhibitor that enhances radiation, chemotherapy and olaparib activity. *Nature Communication 10*, 5065 (2019). https://doi.org/10.1038/s41467-019-12836-9

2. Kyoko Nakamura et al., ; Inhibition of DNA-PK with AZD7648 Sensitizes Tumor Cells to Radiotherapy and Induces Type I IFN-Dependent Durable Tumor Control. *Clin Cancer Res 1* August 2021; 27 (15). https://doi.org/10.1158/1078-0432.CCR-20-3701.

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