Molecularly-informed prediction of treatment efficacy in the GENIE BPC NSCLC cohort using computational reasoning

Barbara Vodicska[1], Eniko Kispeter[1], Dora Lakatos[1], Gabor Gy Kalmar[1], Robert Doczi[1], Dora Gorog-Tihanyi[1], Anna Dirner[1], Reka Szalkai-Denes[1], William T. Beck[2], Arkadiusz Z. Dudek[3], Christophe Le Tourneau[4], Istvan Petak[1]
[1]Genomate Health, Cambridge, MA,[2]University of Illinois at Chicago, Chicago, IL,[3]Division of Oncology, Mayo Clinic, Rochester, MN,[4]Gustave Roussy, Villejuif, France

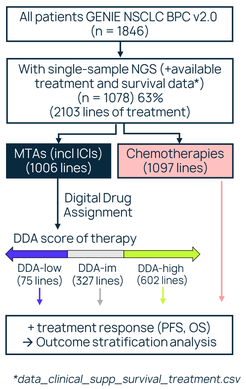
AACR 2026
Poster number: 7

INTRODUCTION

Digital Drug Assignment (DDA) is a computational reasoning model that scores cancer therapies based on the complete molecular profile of a tumor and stratifies them based on predicted efficacy (1). In a prior study of 111 lung cancer patients, DDA-derived high-score molecularly targeted agents (MTAs) were associated with improved clinical outcomes (2). Here, we extend this analysis to the GENIE BPC NSCLC cohort to assess the broader clinical validity of DDA (3, 4).

METHODS

From the GENIE BPC NSCLC cohort data available on Synapse, we included **1,078 patients** with a single-sample genomic profile, available primary treatment data, and survival outcomes (total of 2,103 treatment lines). DDA scores were generated for all cases, and the individual score of the administered MTAs (incl. immune checkpoint inhibitors) was used to stratify outcomes into low (<0), intermediate, and high DDA-score (≥1000) tiers. PFS by imaging and OS were analyzed using Kaplan-Meier statistics.



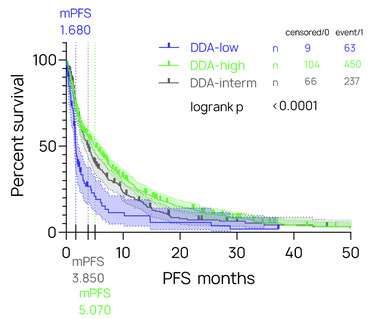
Therapy	lines
MTAs	1006
erlotinib	156
afatinib	46
osimertinib	113
crizotinib	62
pembrolizumab	149
nivolumab	231
atezolizumab	47
ramucirumab+docetaxel	57
bevacizumab+cisplatin+pemetrexed	37
bevacizumab+carboplatin+pemetrexed	108
Chemotherapy	1097
carboplatin+pemetrexed	346
cisplatin+pemetrexed	170
carboplatin+paclitaxel	153
docetaxel	80
cisplatin+vinorelbine	38
pemetrexed	83
gemcitabine	54
cisplatin+etoposide	76
vinorelbine	55
carboplatin+gemcitabine	42

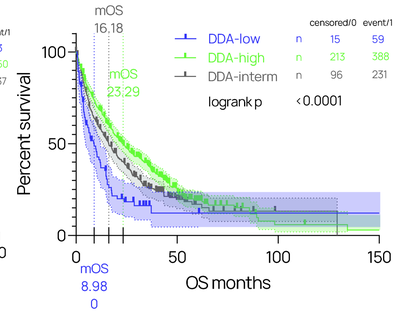
*data_clinical_supp_survival_treatment.csv

RESULTS

PFS and OS stratification

Median PFS and OS differed significantly across DDA score tiers. mPFS increased from 1.7 months in the DDA-low tier to 5.1 months in the DDA-high tier, while median OS increased from 9.0 to 23.3 months. Intermediate-tier drugs had similar mPFS values as chemotherapies, with median PFS of 3.9 months compared to 4.2 months for chemotherapy. The DDA-high tier was associated with reduced risk of progression (HR 0.52) and death (HR 0.49) compared to DDA-low.





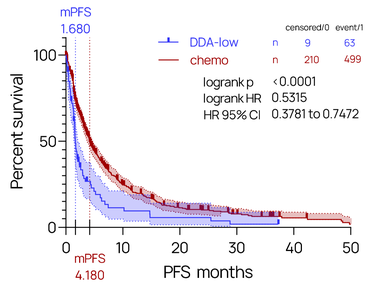
PFS and OS rates

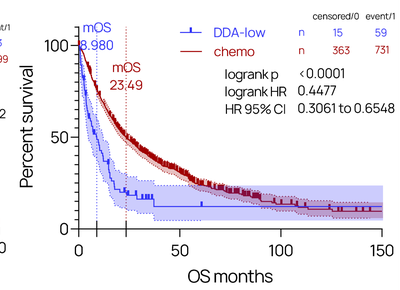
Six-month PFS and twelve-month OS rates increased with DDA-tiers and were all significantly different by χ^2 test. Six-month PFS rates were 14%, 28%, and 40%, while twelve-month OS rates were 36%, 53%, and 63% across DDA-low, -intermediate, and -high tiers, respectively.

	DDA-low	DDA-interm	DDA-high	Statistical test	Chemo
mPFS	1.7 (n = 72)	3.9 (n = 303)	5.1 (n = 554)	log-rank $p<0.0001$; HR high vs low = 0.52	4.2 (n = 709)
mOS	9.0 (n = 74)	16.2 (n = 327)	23.3 (n = 601)	log-rank $p<0.0001$; HR high vs low = 0.49	23.5 (n = 1094)
6-month PFS rate	14%	28%	40%	χ^2 $p<0.0001$	25%
12-month OS rate	36%	53%	63%	χ^2 $p<0.0001$	65%

Benchmark comparison with chemotherapy

PFS was markedly shorter for DDA-low regimens than for chemotherapy (1.7 vs 4.2 months), corresponding to a significantly lower risk of progression on chemotherapy (HR 0.53). A similar pattern was observed for OS (9.0 vs 23.5 months, HR 0.45), supporting the clinical relevance of DDA-based stratification.

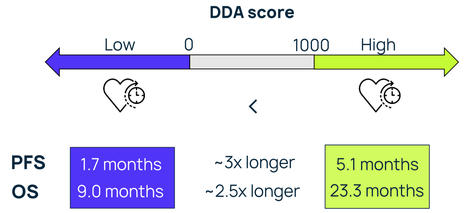




CONCLUSIONS

Take-home messages:

- ✓ DDA stratification distinguishes therapies with higher clinical efficacy in a large, real-world NSCLC cohort.
- ✓ Higher DDA scores are associated with greater clinical benefit across treatment types.
- ✓ DDA-low therapies underperform compared with chemotherapy, highlighting biologically mismatched treatment selection.



DDA provides a scalable approach to therapy prioritization based on comprehensive tumor molecular profiles.

REFERENCES

(1) Petak I et al., npj Precis Onc, 2021
(2) Dirner A et al., npj Precis Onc, 2025
(3) Choudhury NJ et al., Clin Cancer Res., 2023
(4) AACR Project GENIE Consortium, Cancer Discov., 2017

CONTACT

istvan@genomate.health
www.genomate.health

Genomate