

# Cytisinicline in adult smokers: Post-trial survey from ORCA-OL

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| Please add "yes" or "no" to each table cell. If "yes", please turn cell background color to yellow.                     | Tobacco industry  | E-cigarette & nicotine product industry (excluding pharma) | Pharma industry |
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| Off-label medication uses discussed:  | Cytisinicline is a partial agonist/antagonist with selective binding affinity for nicotine receptors and is under investigation for the treatment of nicotine dependence for smoking cessation in adults.             |  |                 |
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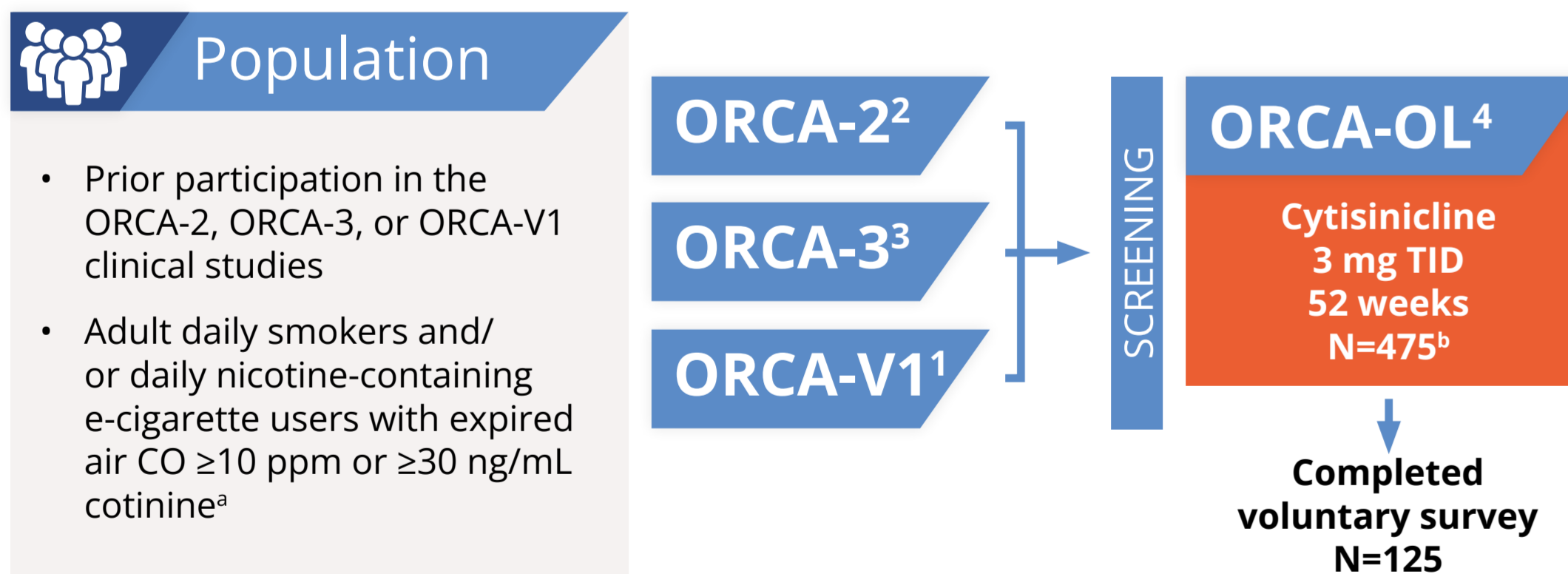
## Introduction

- Cytisinicline is a plant-based alkaloid and partial agonist at  $\alpha 4\beta 2$  nicotinic acetylcholine receptors<sup>1</sup>
- A novel cytisinicline treatment regimen is currently under regulatory review, consisting of a 3 mg tablet administered 3 times daily (TID) for 6 or 12 weeks, as evaluated in the phase 3 ORCA-2 and ORCA-3 trials<sup>2,3</sup>
- In the randomized, placebo-controlled phase 3 ORCA-2 and ORCA-3 trials, cytisinicline was more effective than placebo in achieving continuous smoking abstinence in adults, with a favorable safety profile<sup>2,3</sup>
- In the randomized, placebo-controlled phase 2 ORCA-V1 trial, cytisinicline was more effective than placebo in achieving continuous abstinence from electronic (e)-cigarettes in adults, with a favorable safety profile<sup>1</sup>
- ORCA-OL is a multicenter, open-label (OL) phase 3 study of cytisinicline 3 mg TID for up to 52 weeks in adults who previously took part in the phase 2 (ORCA-V1) or phase 3 (ORCA-2 or ORCA-3) cytisinicline trials<sup>1-4</sup>
- Participants in ORCA-OL were daily cigarette smokers and/or users of daily nicotine-containing e-cigarettes, who were motivated to make another quit attempt<sup>4</sup>

## Objective

To report the findings of a voluntary post-trial participant survey of cytisinicline use during the ORCA-OL trial<sup>4</sup>

## Figure 1. Study design



<sup>a</sup>Using a point-of-care cotinine oral fluid screening device if self-reporting as users of nicotine-containing e-cigarettes; <sup>b</sup>Treated population. CO, carbon monoxide; e-cigarettes, electronic cigarettes; OL, open label; ppm, parts per million; TID, three times daily.

## Materials and methods

- The ORCA-OL study took place at 29 sites across the USA
- Participants were invited to complete a voluntary, post-trial, 15-minute online questionnaire
- After entering their study subject ID, participants completed a structured post-trial survey consisting of closed- and open-ended questions

## Results

### Participants

- Of 475 participants in the ORCA-OL study, 125 completed the voluntary post-trial survey related to cytisinicline use (**Table 1**)

**Table 1. Participants' main source of nicotine at the start of the survey**

| When I started this study, my main source of nicotine was: | Participants (N=125) |
|--|----------------------|
| Cigarettes alone, n (%)                                    | 104 (83)             |
| Nicotine e-cigarettes/vapes, n (%)                         | 16 (13)              |
| Both cigarettes and nicotine e-cigarettes/vapes, n (%)     | 5 (4)                |

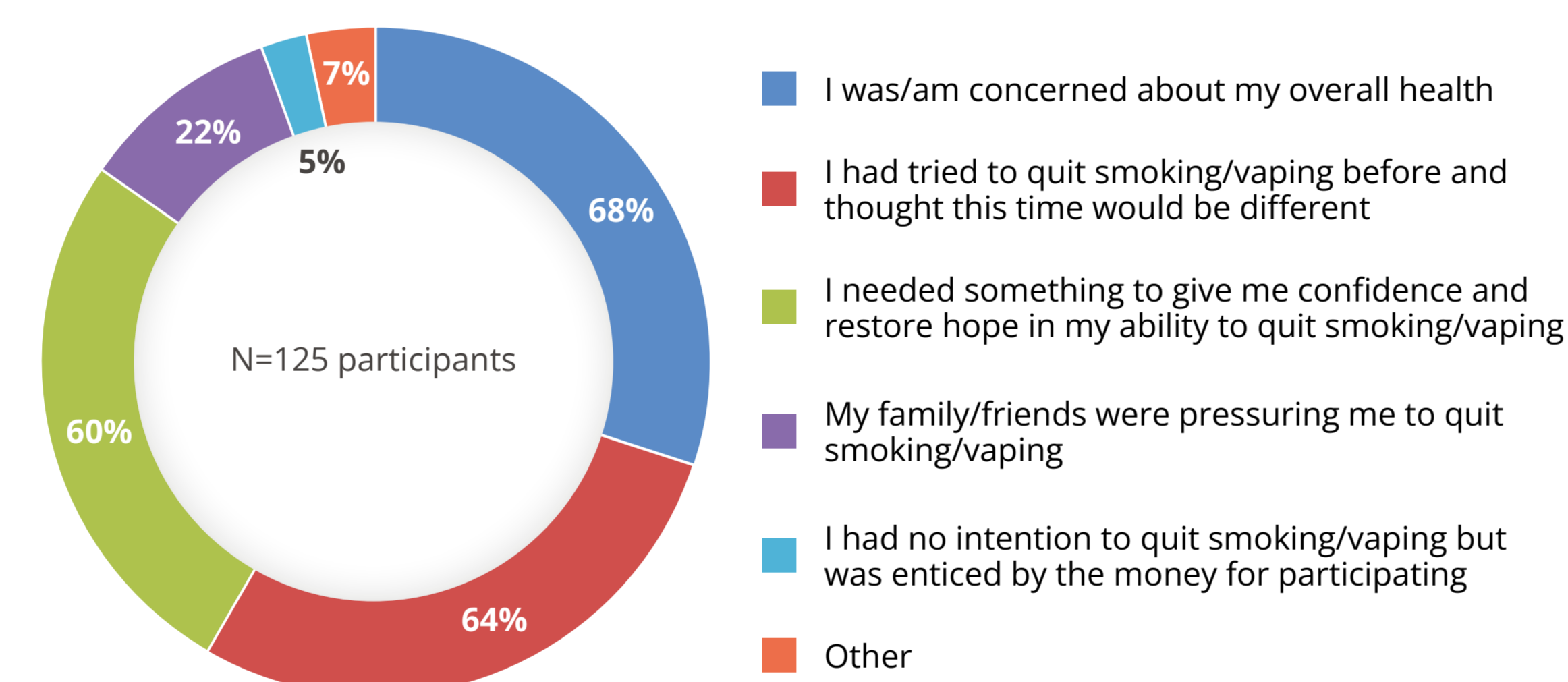
### Treatment expectation:

Participants were optimistic about their ability to quit during ORCA-OL, with over half (55%) expecting to quit and 21% expecting to reduce their smoking and/or vaping

## Figure 2. Survey results

### A. Motivation for trial participation and quitting smoking/vaping

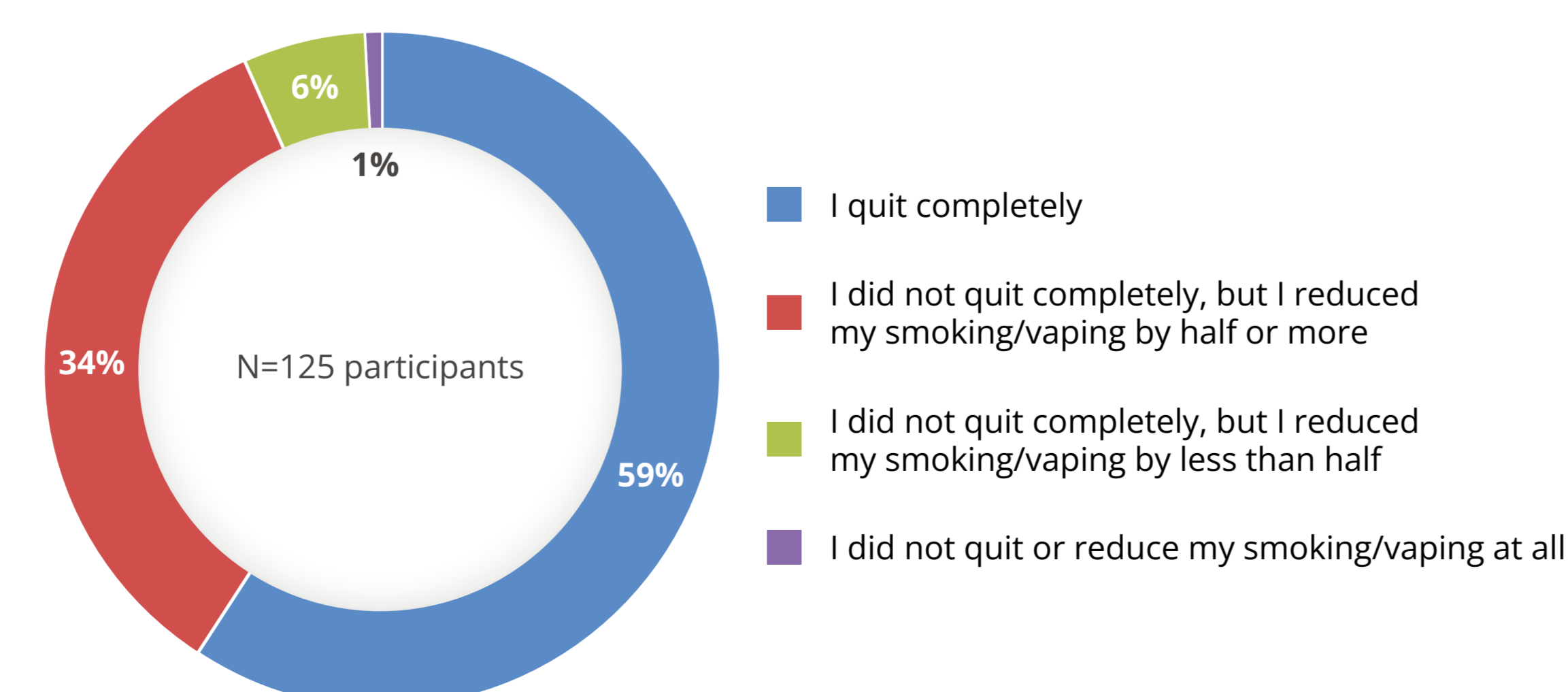
Please select the reasons that you decided to participate in the ORCA-OL trial and to quit smoking or vaping<sup>a</sup>



<sup>a</sup>Participants were permitted to select multiple responses.

### B. Self-reported cessation

Did you completely quit smoking/vaping or reduce smoking/vaping while participating in the ORCA-OL study?



### C. Impressions of the impact of cytisinicline on their nicotine use

Do you believe the study medication contributed to your ability to stop or reduce your nicotine use?

Yes: 98% No: 2%

Please tell us why you selected your answer

"I have seen a dramatic reduction in my desire to smoke as well as no known side effects"

"It absolutely helped. It drastically reduced cravings. There are/were times when I would like to smoke but could easily resist"

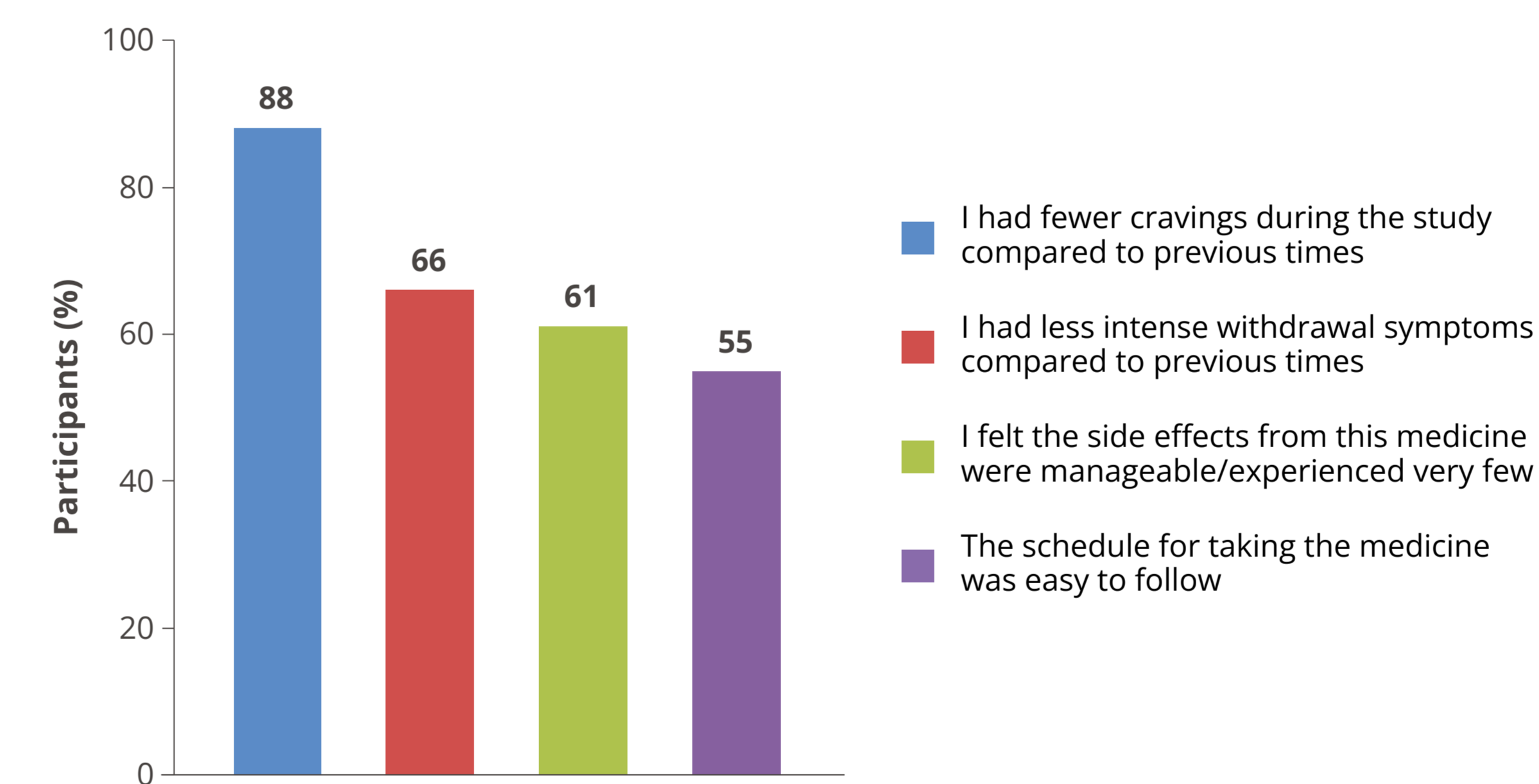
"Literally QUIT even thinking about having a cigarette. ZERO cravings"

"It helped give me the push to quit completely, I'm not sure if I could've done it without the medication"

"I did not experience any physical withdrawals, and when cigarettes are not available or I am in a non-smoking situation, I did not care ... I attribute that to the medicine"

"My vaping reduced. And continued to reduce. I started at 4-6 vapes per month. Now it's only 1"

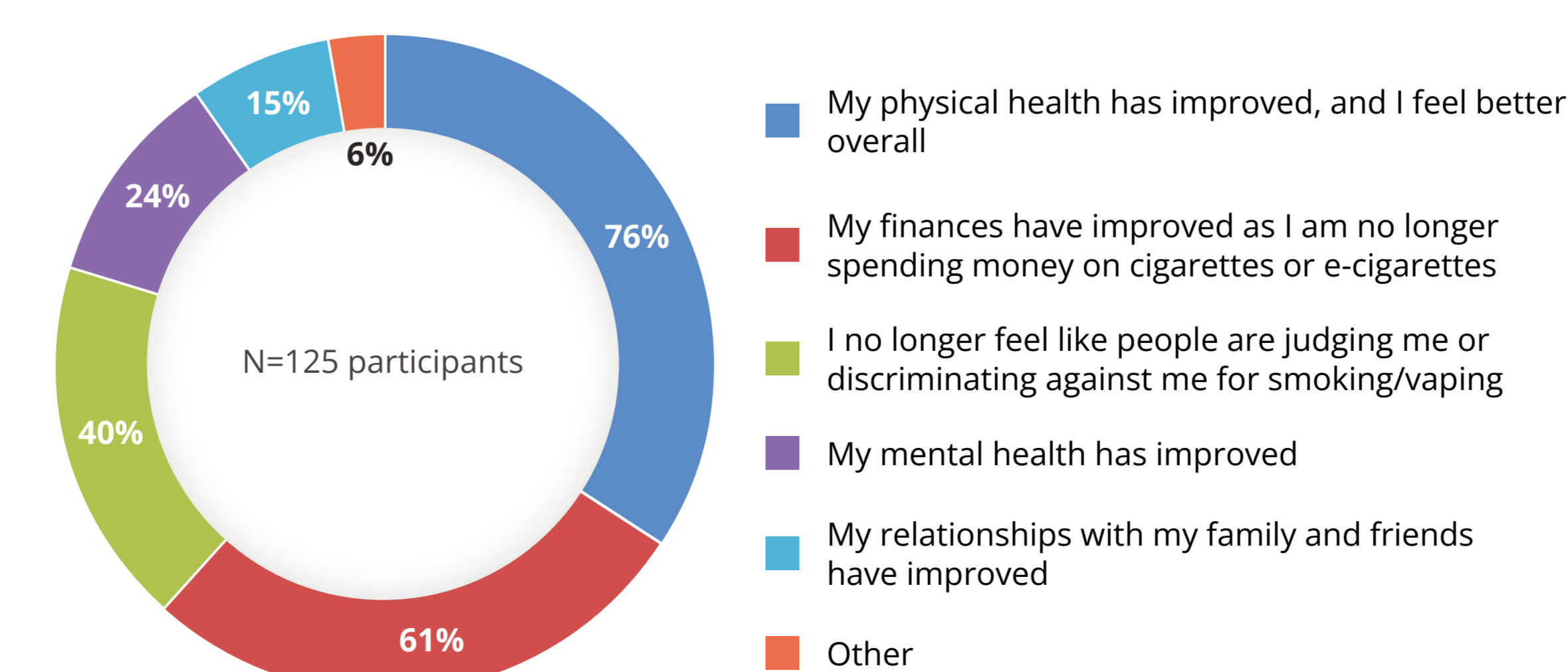
Please select the reasons you believe the medication you received helped you to quit or reduce your smoking/vaping<sup>a,b</sup>



<sup>a</sup>Participants who answered "yes" to question: Do you believe the study medication contributed to your ability to stop or reduce your nicotine use? <sup>b</sup>Participants were permitted to select multiple responses.

### D. Benefits of quitting

If you have quit or reduced smoking/vaping since participating in the ORCA-OL trial, what do you feel are the biggest benefits you have seen or felt so far?<sup>a</sup>



<sup>a</sup>Participants were permitted to select multiple responses.

## Other survey findings

Overall, 98% of participants stated that they would recommend cytisinicline to a friend or family member trying to quit smoking/vaping

## Discussion

- The ORCA-OL study evaluated the safety of long-term, 52-week cytisinicline exposure,<sup>4</sup> whereas the ORCA-2, ORCA-3, and ORCA-V1 studies assessed cytisinicline exposure over 6- and 12-week treatment durations.<sup>1-3</sup> The post-trial survey from ORCA-OL provides exploratory insights into participant experiences with extended cytisinicline use
- Survey participation was limited (125 of 475 ORCA-OL participants),<sup>4</sup> and as a voluntary, open-label survey, results may be biased toward individuals with more positive cessation experiences; self-reported outcomes should be interpreted with appropriate caution
- Findings from this small cohort of long-term exposure participants suggest favorable acceptability of cytisinicline and indicate potential for smoking and vaping cessation, warranting further study<sup>4</sup>

## Conclusions

The findings from this voluntary post-trial survey of cytisinicline use during ORCA-OL showed that most participants reported:

- High quit and reduction rates of nicotine use, driven by fewer cravings
- Manageable or very few side effects
- Broad perceived benefits
- They would recommend cytisinicline to others

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**References:** 1. Rigotti NA et al. JAMA Intern Med. 2024;184:922-30; 2. Rigotti NA et al. JAMA. 2023;330:152-60; 3. Rigotti NA et al. JAMA Intern Med. 2025;185:648-55; 4. Available at: <https://clinicaltrials.gov/study/NCT06435221>