Article

Awareness of Medication-Related Osteonecrosis of the Jaws amongst Dental Professionals in Poland

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Abstract: Background: Medication-Related Osteonecrosis of the Jaws (MRONJ) is a serious complication of antiresorptive therapy. The aim of the study was to assess the level of knowledge and awareness regarding MRONJ among Polish dentists and students of dentistry. Methods: The online self-administered questionnaire was sent out electronically among dentists in Poland and dentistry students of the Medical University of Gdansk. The results obtained were statistically analyzed. The results were considered statistically significant if the condition $p \leq 0.05$ was met. Results: A total of 203 respondents participated in this survey. A total of 94.6% of them declared knowledge of the term MRONJ. However, the length of bisphosphonates persistence in the body was known to 51.5% of participants, while the knowledge of oral and maxillofacial surgeons concerning this topic was significantly higher (87.0%). Conclusion: Dental and maxillofacial surgeons presented the highest level of knowledge about MRONJ. The remaining groups did not differ in their knowledge. It must be noted that the knowledge of the students was similar to that of dentists. A better level of knowledge by dentists could contribute to a decline of the occurrence of the disease in future. Theoretical and practical initiatives should be promoted to improve the knowledge about MRONJ.

Keywords: osteonecrosis; bisphosphonates; antiresorptive agents; awareness; knowledge; dentist

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1. Introduction

Dentists are increasingly confronted with the occurrence of Medication-related Osteonecrosis of the Jaw (MRONJ), which is a serious complication in the treatment of diseases characterized by an excessive bone resorption. Antiresorptive drug therapy is currently widely used in treatment of patients suffering from osteoporosis, Paget's disease and osteogenesis imperfecta, as well as in the treatment and prevention of neoplastic metastases associated with breast, prostate and lung cancer and multiple myeloma. According to the current literature, medication-related osteonecrosis of the jaw is a serious complication not only in the therapy using drugs belonging to the bisphosphonate group, but also with denosumab and angiogenesis inhibitors [1–4]. Due to this, in 2014, the American Association of Oral and Maxillofacial Surgeons (AAOMS) proposed changing the term from Bisphosphonate Related Osteonecrosis of the Jaw (BRONJ) to Medication-Related Osteonecrosis of the Jaw (MRONJ) [1].

As of today, no effective methods of treating MRONJ have been developed; therefore, the prevention of this disease is of key importance [5,6]. Prophylactic management is determined by the prior assessment of the risk level of MRONJ and the type and duration of antiresorptive treatment [2,7–10]. Prior to the commencement of antiresorptive treatment, regardless of their

respective risk group, patients should undergo a comprehensive dental examination, including radiological diagnostics, and receive oral hygiene instructions [2–4,11,12].

Dentists should be prepared to treat patients at risk of medication-related osteonecrosis of the jaw and they may be the first physicians able to recognize the initial symptoms of MRONJ. Current knowledge about this disease is essential in the work of a dentist. The literature on the awareness of dentists and students of dentistry is scarce [13–19]. The aim of this study was to assess the level of knowledge and awareness regarding MRONJ among Polish dentists and students of dentistry.

2. Materials and Methods

This descriptive cross-sectional study was performed using a web-based structured questionnaire among dental professionals working in Poland as well as 4th and 5th year dental students of the Medical University of Gdansk (MUG). The online self-administered questionnaire including a cover letter explaining the purpose of study was sent out electronically in March 2020. Answers were obtained until the end of September 2020. The anonymous survey consisted of two parts: part I evaluated the demographic and professional data including age, years of experience, specialization and a type of working sector; part II assessed knowledge about MRONJ. To maintain total confidentiality, participants were not required to write down their names in the questionnaire. The study included 103 dentists from multiple cities in Poland and 100 dentistry students of the MUG (Appendix A).

Statistical Analysis

In order to implement the premise of the study, a statistical analysis of the collected data was used. It was conducted by means of Statistica software, version 13.1 PL. The general characteristics of the information collected in the questionnaire were determined with the help of frequency statistics, i.e., the number of cases that meet a particular condition and the calculation of their percentage share in relation to the total number of respondents.

Additionally, the general knowledge score, as the sum of the correct answers, was calculated for each subject. The resulting variable was subjected to the analysis of the normality of the distribution, which was carried out by means of the Kolmogorov–Smirnov and W Shapiro–Wilk tests. Intergroup comparisons in terms of variables whose results were described on the nominal scale (correct or wrong answer to the survey question) were made by means of the Pearson chi-square test of independence. Parametric tests were used for the quantitative variable, which was the point knowledge score. Student's t-test was used for comparisons between two independent groups and, for comparisons of more independent groups ($k > 2$), a one-way ANOVA F test was used. If a statistically significant result was found, a post hoc analysis was performed by means of the Scheffe test. The level of statistical significance in the study was $\alpha = 0.05$. This means that the results of the 84 analyses were considered statistically significant if the condition $p \leq 0.05$ was met.

3. Results

All participants were divided into four groups to evaluate their knowledge about BP and MRONJ. The first group (group G1) included oral and maxillofacial surgeons, the second group (group G2) consisted of other specialists in dentistry and the third group (group G3) comprised of general dental practitioners. The fourth group (group G4) included dentistry students in the 4th and 5th year of the MUG's. Figure 1 presents the distribution of all participants who responded to the survey. The ratio of dentists belonging to group G2, that is: specialists in fields other than dental surgery and maxillofacial surgery, is presented in Figure 2. The participants, with the exception of students, were further divided into work sectors (Figure 3) and according to years of experience (Table 1).

The results of the survey of dentists and dental students concerning the knowledge about BP, MRONJ and assessing behavior in clinical situations are shown in Tables 1–5.

Figure 1. The distribution of participants who responded to the survey.

Figure 2. The number of the specialists in fields other than dental surgery and maxillofacial surgery (group G2).

Among the 200 respondents, 94.6% of them declared knowledge of the term MRONJ, and in their clinical practice less than half of the respondents (47.0%) encountered medication-related osteonecrosis of the jaw. A total of 69.7% correctly defined the clinical picture of osteopathy visible in the oral cavity, including 82.6% from the G1 group, who are specialists in the field of dental and maxillofacial surgery. In the remaining groups, the number of correct answers to this question is lower and amounts to: G2—63.2%, G3—66.7%, G4—67.7% (Table 1).

Only 60.9% oral and maxillofacial surgeons (G1) were aware of drugs correlated with Medication-Related Osteonecrosis of the Jaw, whereas the knowledge of the rest of the participants was at a significantly lower level. It is disturbing to note a very low level of knowledge among dentists who work in the private sector—only 16.0%. It must be noted that dentists who work exclusively in the private sector also encounter MRONJ more rarely (24.0%) in their practice than their colleagues working in both the public and private sector (64.6%) and their knowledge of MRONJ symptoms is lower (58.0%) (Table 1).

Figure 3. Division of dentists participating in the survey depending on their professional field.

Most of the participants knew the principal disease entities treated with BP such as osteoporosis, bone metastases and multiple myeloma. Besides the above mentioned diseases, the less-frequently known osteogenesis imperfecta was not recognized as well (Table 2).

Most of the participants were aware of how to administer BP—oral and IV (93.1%) and of the necessity of oral sanitation before BP treatment is fundamental (96.0%) (Table 3). The importance of referral to the dentists before BP therapy were perceived by 95.7%, 94.7%, 93.3% and 96.0% of groups G1, G2, G3 and G4, respectively. However, the length of BP persistence, which is predicted as up to 10 years in the organism, were known in less than 50% in groups G2 (42.1%) and G3 (36.7%), slightly more in group G4 (52.5%), whilst the knowledge of oral and maxillofacial surgeons (group G1) about this topic was significantly higher and 87.0% of respondents in this group gave the correct answer to this question.

When asked about the increased risk of MRONJ in the case of intravenous (IV) administration of BP, 58.9% of all participants gave the correct answer. Moreover, taking into account the specialization of the respondents, as many as 91.3% of surgeons answered this question correctly. In the remaining groups the results were lower, G2—42.1%, G3—53.3%, G4—57.6%, respectively. Interestingly, the results of the analysis of the survey showed that 34.2% of the study participants admitted that they did not know the answer, and 6.9% answered incorrectly.

Furthermore, participants presented their knowledge regarding MRONJ—treatment recommendations, risk factors and guidelines (Tables 4 and 5). Periodontal disease (93.1%) and poor oral hygiene (93.1%) was the best recognized risk factor of MRONJ. However, only below 60% of the dentists in groups G2 and G3 and students knew the importance of the way of BP administration for MRONJ occurrence. Dental specialists in oral and maxillofacial surgery showed better comprehensive knowledge of risk factors, but insufficient for steroid therapy and tobacco use. It is surprising that only 37.4% of students pointed to alcohol as an incorrect answer, which is the lowest result among all examined groups. Detailed results are shown in Table 4.

Table 1. General knowledge about MRONJ.

General Knowledge about MRONJ	Total (<i>n</i> = 200)	Examined Groups:					The Duration of Work experience (Years):				Dentists in Work Sector:		
		G1 (<i>n</i> = 23)	G2 (<i>n</i> = 19)	G3 (<i>n</i> = 60)	G4 (<i>n</i> = 98)	<i>p</i>	<1y (<i>n</i> = 4)	1–10y (<i>n</i> = 79)	11–20y (<i>n</i> = 17)	<i>p</i>	Public and Private (<i>n</i> = 50)	Private (<i>n</i> = 47)	<i>p</i>
Participants (%) familiar with definition of MRONJ	94.6%	100%	100%	86.7%	97.0%	0.014	100%	89.9%	100%	NS	93.8%	90.0%	NS
Participants (%) who encountered MRONJ in practice	47.0%	87.0%	42.1%	28.3%	51.0%	0.00003	25.0%	43.0%	52.9%	NS	64.6%	24.0%	0.00005
Participants (%) who know the symptoms of MRONJ	69.7%	82.6%	63.2%	66.7%	67.7%	NS	100%	69.6%	58.8%	NS	79.2%	58.0%	0.02429
Participants (%) who know drugs which are responsible for the risk of developing MRONJ	33.7%	60.9%	31.6%	26.7%	30.3%	0.02298	50.0%	36.7%	23.5%	NS	54.2%	16.0%	0.00007

Intergroup comparisons in terms of variables whose results were described on the nominal scale (correct or wrong answer to the survey question) were made by means of the Pearson chi-square test of independence. NS—non-significant.

Table 2. Answers to the question concerning the diseases treated with bisphosphonates.

Participants (%) with	Total	Examined Groups:				
Knowledge about Diseases	(<i>n</i> = 201)	G1 (<i>n</i> = 23)	G2 (<i>n</i> = 19)	G3 (<i>n</i> = 60)	G4 (<i>n</i> = 99)	<i>p</i>
Treated with BP:						
Osteoporosis	93.6%	100%	89.5%	93.3%	93.9%	NS
Multiple Myeloma	66.5%	91.3%	63.2%	56.7%	67.7%	0.02757
Bone metastases	84.2%	100%	68.4%	80.0%	86.9%	0.02489
Paget’s disease of bone	57.1%	52.2%	63.2%	50.0%	62.6%	NS
Osteogenesis imperfecta	19.7%	17.4%	15.8%	23.3%	18.2%	NS

Intergroup comparisons in terms of variables whose results were described on the nominal scale 154 (correct or wrong answer to the survey question) were made by means of the Pearson chi-square test of 155 independence. NS—nonsignificant.

Table 3. General knowledge about bisphosphonates.

Correct Answers of the Participants (%) to Questions Concerning:	Total (<i>n</i> = 202)	Examined Groups:				<i>p</i>
		G1 (<i>n</i> = 23)	G2 (<i>n</i> = 19)	G3 (<i>n</i> = 60)	G4 (<i>n</i> = 100)	
BP's administration (oral and IV)	93.1%	100%	89.5%	88.3%	93.9%	NS
Dental check before BP treatment (Yes)	96.0%	95.7%	94.7%	93.3%	96.0%	NS
Length of BP persistence in the organism (10 years)	51.5%	87.0%	42.1%	36.7%	52.5%	0.00055
Greater risk of MRONJ due to oral administration versus intravenous (IV is higher)	58.9%	91.3%	42.1%	53.3%	57.6%	0.00462

Intergroup comparisons in terms of variables whose results were described on the nominal scale (correct or wrong answer to the survey question) were made by means of the Pearson chi-square test of independence. NS—nonsignificant.

Table 4. Risk factors of MRONJ.

Answers of Participants (%) to the Question about of MRONJ Risk Factors	Total (<i>n</i> = 202)	Examined Groups:				<i>p</i>
		G1 (<i>n</i> = 23)	G2 (<i>n</i> = 19)	G3 (<i>n</i> = 60)	G4 (<i>n</i> = 100)	
Poor Oral Hygiene (correct)	93.1%	100%	84.2%	95.0%	91.9%	NS
Periodontal Disease (correct)	93.1%	100%	84.2%	95.0%	91.9%	NS
Denture wearing (correct)	82.3%	78.3%	79.0%	81.7%	83.8%	NS
Tobacco use (correct)	80.8%	65.2%	84.2%	80.0%	83.8%	NS
Steroid therapy (correct)	54.7%	43.5%	63.2%	50.0%	58.6%	NS
Length of therapy (>3y)	75.9%	87.0%	79.0%	73.3%	74.8%	NS
Manner of administration (IV)	56.7%	82.6%	57.9%	53.3%	52.5%	NS
Hypertension (incorrect)	84.7%	95.7%	79.0%	88.3%	81.8%	NS
Hyperlipidemia (incorrect)	80.3%	91.3%	84.2%	78.3%	77.8%	NS
Alcohol (incorrect)	47.3%	60.9%	57.9%	55.0%	37.4%	0.04822

Intergroup comparisons in terms of variables whose results were described on the nominal scale (correct or wrong answer to the survey question) were made by means of the Pearson chi-square test of independence. NS—nonsignificant.

Table 5. The knowledge about MRONJ.

Knowledge about MRONJ	Total (<i>n</i> ¹ = 200) (<i>n</i> ² = 201)	Examined Groups:				<i>p</i>
		G1 (<i>n</i> = 23)	G2 (<i>n</i> = 19)	G3 (<i>n</i> = 60)	G4 (<i>n</i> ¹ = 97) (<i>n</i> ² = 98)	
Participants (%) who declare that they know the guidelines of MRONJ treatment	55.2%	87.0%	26.3%	41.7%	60.8%	0.00009
Participants (%) who want to know more about MRONJ	96.0%	95.7%	89.5%	96.7%	98.0%	NS

Intergroup comparisons in terms of variables whose results were described on the nominal scale (correct or wrong answer to the survey question) were made by means of the Pearson chi-square test of independence. NS—nonsignificant. *n*¹—Number of participants who answered the question: “Do you know the guidelines for managing patients at risk of developing MRONJ?”. *n*²—Number of participants who answered the question: “Would you like to know more about MRONJ?”.

Only a little more than half of surveyed participants (55.2%) declare that they know the guidelines of MRONJ treatment (Table 5). In the results there is a visible disproportion in answers to this question between groups G1 and G2. The acquaintance of guidelines for the treatment and prophylaxis of MRONJ were declared by 87.0% of the surveyed specialists in the field of dental and maxillofacial surgery (group G1). However, specialists in other fields of dentistry (group G2) achieved the lowest results, which means that only 26.3% of dentists in this group declare knowledge of these guidelines. It is encouraging that 96.0% of the study participants would like to know more about MRONJ (Table 5).

4. Discussion

To the best of our knowledge, this is the first study assessing MRONJ knowledge among dental practitioners and dentistry students from Poland. Comparing the obtained results with those from similar studies carried out in other countries, responses of participants in our study are on a satisfactory level and stand out positively compared to other surveys [13,15,19,20].

On the basis of the survey, 94.6% of respondents stated that they know the term MRONJ, which is the highest result among other studies conducted so far. Jaw-bone osteonecrosis associated with the use of bisphosphonates and other antiresorptive drugs (MRONJ) is widely regarded as one of the most serious complications in the treatment of diseases characterized by an excessive bone resorption. Currently, there is no effective treatment for MRONJ and therefore the key is the prevention of this disease and the management of the recommended therapeutic strategies in relation to the advancement of MRONJ [5,6]. The results concerning the level of knowledge of MRONJ guidelines seem alarming, as only 26.3% of the surveyed dentists of other specialties (group G2) declared knowledge of these guidelines, and in the remaining groups (G3 and G4) the results are only slightly higher. Only specialists in the field of dental and maxillofacial surgery report a significantly higher degree of knowledge of procedures for the treatment of patients with this osteopathy (87.0%). This may result from the specificity of the specialization, which is associated with a greater likelihood of contact with patients suffering from MRONJ. According to the results of the study, 87.0% of the surveyed dental and maxillofacial surgeons reported having prior contact with a patient with MRONJ symptoms.

It is also interesting that dentists working in the public sector show more knowledge in this area, which may be related to the implementation of specialization, which in Poland takes place mainly in the public sector. On the other hand, the study showed that seniority has no significant impact on the level of knowledge about MRONJ.

Due to the expansion of medical indications for therapy with bisphosphonates and other antiresorptive drugs (e.g., denosumab), the number of patients suffering from MRONJ has increased significantly [1,21]. The results show that although 94.6% of respondents know about the existence of such a disease, only 33.7% know that BP, denosumab and angiogenesis inhibitors are drugs that increase the risk of MRONJ. In the research of Franchi, who assessed the knowledge of medical students in Italy in his study, out of 72 respondents, only 12 (16.7%) possessed knowledge about the type of drugs that increased the risk of MRONJ [20]. Without this crucial knowledge about therapeutics, the risk of treatment complication is elevated. One third of the respondents indicated only bisphosphonates, which may be the result of the knowledge of the publication on bisphosphonate-related bone necrosis (BRONJ), which was first described in 2003 by Marx et al. [22]. However, in 2014, the AAOMS proposed the use of the term MRONJ due to the increasing number of reported cases of osteonecrosis of the jaws associated with other antiresorptive drugs [1]. According to the survey evaluating the awareness of MRONJ within the Birmingham GMP community, only 6% of participants were aware of change in terminology from BRONJ to MRONJ [23]. Without a thorough knowledge of drugs used in antiresorptive therapies, dentists may contribute to an increased risk of developing MRONJ by not following the recommendations in patients at risk of osteonecrosis of the jaws [3,24].

The 2014 AAOMS criteria indicate that a patient may be suspected of MRONJ if all of the following conditions are met: current antiresorptive or antiangiogenic drug therapy or past history of such treatment; exposure of the craniofacial bones or intra- or extraoral fistula in this area-lasting for more than 8 weeks; no history of radiation therapy to the jaws; no neoplastic metastases to the jaw bones [1]. Clinical signs may present a bare or necrotic jaw bone, pathological fracture, pain, inflammation, tooth mobility, intra- or extraoral fistula [1,21,25]. A total of 69.7% of the respondents correctly indicated the description of the clinical picture of MRONJ in the oral cavity, among which the vast majority of correct answers were provided by those specializing in surgery (82.6%). Typically, osteonecrosis is caused by a preceding local infection or damage to the oral mucosa or bone [2,3]. The most

frequently presented risk factors in the oral cavity are tooth extraction (45%), periodontal disease (10%) and poorly fitted removable prosthetic restorations [3,24,26,27].

Before starting antiresorptive treatment, patients should undergo a dental examination and receive oral hygiene instruction [2,4,11,12]. A total of 193 surveyed dentists and students of dentistry (96.0%) are aware of the necessity of oral cavity sanitation before starting bisphosphonate treatment, which indicates the need for cooperation between doctors and dentists. Researchers in Brazil achieved a slightly lower result, where 87.69% and 84.59% of the dentists and physicians surveyed, respectively, indicated the importance of referral to a dentist before starting therapy with antiresorptive drugs [28]. In a UK study of general medical practitioners (GMPs), although more than half of them present a risk of MRONJ to their patients, only 32% consider referral to a dentist before prescribing antiresorptive drugs [23]. Researchers in Italy obtained much more promising results on this subject among students of the last two years of medicine. Almost all students (71 out of 72 respondents) replied that a dental examination was needed before starting bisphosphonate therapy [20]. Better education on this subject during medical studies may result in greater awareness of the prevention, risk factors and management of MRONJ among young physicians.

5. Conclusions

In our survey, dentists specializing in dental and maxillofacial surgery exhibited the highest degree of knowledge about MRONJ. The remaining groups did not differ in their level of knowledge between each other. The duration of work experience does not translate into greater knowledge about MRONJ. It is noteworthy that the dentists working in the private sector have less contact with patients suffering from MRONJ, which translates into a lower level of knowledge about this disease than the dentists working in both the public and private sector. It must be emphasized that the knowledge of the students was similar to that of practicing dentists. The quality of education received by the students of MUG on the topic of MRONJ is reasonably high. Providing students with adequate education about MRONJ could be major aspect of MRONJ prevention in the future.

Considering the results of the study, it is advisable to further promote the knowledge about prophylaxis and dental preparation of patients for the implementation of antiresorptive treatment, e.g., in the form of generally accessible trainings, studies or webinars. It is encouraging that the majority of respondents declared a desire to know more about MRONJ which, in turn, could contribute to a decline of the occurrence of the disease in the future.

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Conflicts of Interest: The authors declare no conflict of interest.

Appendix A

Questionnaire—Awareness of Medication-Related Osteonecrosis of the Jaws amongst Dental Professionals in Poland.

I General Information

1. Age

- ☐ <25
- ☐ 25–35
- ☐ 35–50
- ☐ >50
- 2. Years of professional experience
 - ☐ <1
 - ☐ 1–10
 - ☐ 11–20
 - ☐ >20
 - ☐ Student
- 3. Dental specialization
 - ☐ General Dentistry
 - ☐ Oral Surgery
 - ☐ Conservative Dentistry and Endodontics
 - ☐ Periodontology
 - ☐ Prosthodontics
 - ☐ Maxillofacial Surgery
 - ☐ Pedodontics
 - ☐ Orthodontics
 - ☐ Student
- 4. Work sector
 - ☐ Public
 - ☐ Private
 - ☐ Public and private
 - ☐ Student

II. General Knowledge about MRONJ

- 1. In what diseases is bisphosphonate treatment used? (please mark all that apply)
 - ☐ Osteoporosis
 - ☐ Multiple myeloma
 - ☐ Cancer metastases to the bone
 - ☐ Anemia
 - ☐ Osteogenesis imperfecta
 - ☐ Paget's disease
 - ☐ Hypertension
- 2. In what way are bisphosphonates administered?
 - ☐ Intravenously
 - ☐ Orally
 - ☐ Intravenously and orally
 - ☐ I don't know
- 3. Is a dental examination and oral cavity sanitation necessary before starting bisphosphonate therapy?
 - ☐ Yes
 - ☐ No
 - ☐ It does not matter
- 4. Are you familiar with the term MRONJ—Medication Related Osteonecrosis of the Jaw?
 - ☐ Yes
 - ☐ No
- 5. Which drugs are responsible for the risk of developing MRONJ?
 - ☐ Bisphosphonates
 - ☐ Bisphosphonates and Denosumab

- ☐ Bisphosphonates and Angiogenesis Inhibitors
 - ☐ Bisphosphonates, Denosumab and Angiogenesis Inhibitors
 - ☐ I do not know
6. What is the clinical picture of MRONJ in the oral cavity?
- ☐ Exposed bone necrosis
 - ☐ Bone necrosis outbreak without bone exposure
 - ☐ Bone necrosis outbreak with or without bone exposure
 - ☐ I don't know
7. Do you know the guidelines for managing patients at risk of developing MRONJ?
- ☐ Yes
 - ☐ No
8. Does oral ingestion of bisphosphonates carry a greater risk of developing MRONJ than if administered intravenously?
- ☐ Yes
 - ☐ No
 - ☐ I don't know
9. How long after completing bisphosphonate therapy are bisphosphonates present in the organism?
- ☐ Up to 1 month
 - ☐ Up to 6 months
 - ☐ Up to 1 year
 - ☐ Up to 10 years
10. Do you know what are the risk factors for MRONJ? (please mark all that apply)
- ☐ Alcohol
 - ☐ Smoking cigarettes
 - ☐ Poor oral hygiene
 - ☐ Periodontal disease
 - ☐ Poorly fitted removable prosthetic restorations
 - ☐ Hyperlipidemia
 - ☐ Steroid therapy
 - ☐ Length of therapy
 - ☐ Method of administration (oral/intravenous)
 - ☐ Hypertension
11. Have you encountered MRONJ in your practice?
- ☐ Yes
 - ☐ No
12. Would you like to know more about MRONJ?
- ☐ Yes
 - ☐ No
 - ☐ I do not know

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